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A CONCEPTUALISATION OF A GOVERNANCE MODEL FOR BIOBANKS IN THE DIGITAL SOCIETY

Presentata da: Sofia Iacomussi

Supervisore:
Michele Graziadei

Coordinatore Dottorato:
Monica Palmirani

Co-supervisore:
Itziar De Lecuona

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A Pablo e Olivia

Abstract

Biobanks are key infrastructures in data-driven biomedical research. They provide a systematic and high-quality collection of well-annotated human biological materials and updated biomedical databases to the scientific community. Their contribution is fundamental in supporting the goal of translational research to make a real impact on the delivery of healthcare and to provide new inputs for personalised medicine.

The counterpoint of this optimistic vision is the reality of biobank governance, which must address various ethical, legal and social issues, especially in terms of open consent, privacy and secondary uses which, if not sufficiently resolved, may undermine participants' and society's trust in biobanking. The effect of the digital paradigm on biomedical research has only accentuated these issues by adding new pressure for the data protection of biobank participants against the risks of covert discrimination, abuse of power against individuals and groups, and critical commercial uses. Moreover, the traditional research-ethics framework has been unable to keep pace with the transformative developments of the digital era, and has proven inadequate in protecting biobank participants and providing guidance for ethical practices. To this must be added the challenge of an increased tendency towards exploitation and the commercialisation of personal data in the field of biomedical research, which may undermine the altruistic and solidaristic values associated with biobank participation and risk losing alignment with societal interests in biobanking.

My research critically analyses, from a bioethical perspective, the challenges and the goals of biobank governance in data-driven biomedical research in order to understand the conditions for the implementation of a governance model that can foster biomedical research and innovation, while ensuring adequate protection for biobank participants and an alignment of biobank procedures and policies with society's interests and expectations. Accordingly, my thesis aims to contribute to the conceptualisation of a socially-oriented and participatory model of biobanks by proposing a new ethical framework that relies on the principles of transparency, data protection and participation to tackle the key challenges of biobanks in the digital age and that is well-suited to foster these goals.

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Contents

List of Abbreviations

ELSI Ethical Legal and Societal Issues

GDPR General Data Protection Regulation

ICTs Informatic and Communication Technologies

RECs Research Ethics Committees

RRI Responsible Research and Innovation

WMA World Medical Association

Introduction

Biobanks are key infrastructures in the most cutting-edge advances in biomedical research, such as translational research and personalised medicine, to which they contribute by providing researchers with high-quality and well-annotated human biological samples and associated databases containing genetic, biological and other health-related information to help translate this information into clinically relevant outcomes for the benefit of public health.

In 2009, Time Magazine listed biobanks as among the 'ten ideas changing the world right now'.[1] By that time, the growth of biobanking had brought many benefits to different areas of biomedical research, enabling progress in the earlier detection of diseases, more effective treatments, prevention, prediction and new inputs for personalised medicine.

In recent years, the emergence of the digital paradigm in biomedical research, brought about as a result of the transition from the analogue to the digital society, has given an additional boost to the field of biobanks, elevating them to the main source for the collection and sharing of biomedical datasets, essential for data-driven research.

Such a promising endeavour brings with it many ethical, legal and societal issues, related to the difficulty in finding a balance between the rights of individuals who participate with their biological samples and personal data, and the broader public interests and research goals. On the one hand, some issues are inherent to the concept of biobanking itself, that is, collecting samples and data for future purposes and these, in turn, have consequences for participants' privacy, protection, and the role of informed consent in protecting the autonomy of individuals involved in research. On the other hand, to this class of ethical, legal and societal issues, we can now add the new challenges brought by data-driven research. From a practical point of view, biobank samples and associated data are sought by researchers precisely because they can be re-used and re-purposed multiple times. The ethical conflict arises because biobanks collect, use and share sensitive personal data for a research context defined by the digital paradigm, whose limited ability to control

[1] Available at: http://content.time.com/time/specials/packages/article/0,28804,1884779_1884782_1884766,00.html [Accessed 4 April 2022]

anonymisation, the possibility of linking datasets of a different nature and the transferability of health data in other domains endangers individuals' privacy, exposing them to the risks of covert discrimination, unwanted commercial use and abuse of power against individuals or groups.

These ethical legal and societal issues associated with biobanks need to be read in the light of the leading values and trends that define the digital society today. That is to say, biobanks operate in a context that responds to clear political, economic and societal commitments to a data-driven economy based on the exploitation and commercialisation of personal data. Given that such trends have reached the context of biomedical research, biobanks today need to face the ethical, legal and societal issues brought by the new logic of the health-data marketplace.

Given this context, to ensure viability over time and to maintain public trust, biobank governance needs to find a way to ensure the protection of participants and respect for their rights while providing a high-quality service to meet the needs of the scientific community.

This challenge is complicated by the fact that the normative framework applicable today to biobanks in Europe presents several weaknesses, for two distinct reasons. Regarding regulation, the situation is very fragmented, since few states have implemented bespoke legislation for biobanks, with most relying on non-binding guidelines or soft tools.

As regards ethical guidance, the bioethical reference texts that provided the basis for research ethics in an analogue society have demonstrably failed to offer support on current issues, such as different models of consent other than specific, secondary uses of samples and confidentiality.

The stakes are, therefore, very high. In biobanking, we are talking of a phenomenon that is central to the progress of biomedical research, but whose potential is not sufficiently supported by an ethical and legal framework able to accommodate the ethical, legal and societal issues raised in data-driven biomedical research.

Accordingly, the goal of my dissertation is to design an ethical framework for biobank governance that ensures a balance between the beneficial applications of data-intensive biomedical research, understood as practices centred on the massive collection and

processing of personal data, and adequate protection of biobank participants against current risks and harms.

To this end, this thesis takes up the challenge to conceptualise an adequate governance for biobanks in data-driven biomedical research from a bioethical and philosophical perspective, thus responding to a clear moral mandate to consider and suggest the direction that the digital society should follow as regards biomedical research and innovation. In other words, what is the most ethical direction that a society fed by personal data – and accustomed to its exploitation and commercialisation – can take?

Throughout this work, I suggest that the right direction is that aligned with the values and expectations of society and, at the same time, able to protect research participants – and in turn, society itself – against the many risks associated with the digital paradigm, such as covert discrimination, abuse of powers against individuals and groups and unwanted secondary use of personal data. Furthermore, it must protect both participants and society against certain political, economic and social trends that endanger the constitutional values associated with research, given that price tends to prevail on the value of research.

In brief, the challenge of conceptualising a governance model for biobanks in the digital age reflects much higher stakes, because it reflects on a micro-scale one of the pressing questions of our century – the responsibility of shaping digital innovation in a way that is ethical and aligned with the interests of the largest possible number of societal actors.

1. Approach and Objectives

The nature of my contribution is a conceptual analysis and redefinition of the problem as a response to the challenges faced by biobank governance in the digital society basis on my expertise in philosophy and bioethics. The model of governance and the set of principles that I propose are intended to help reframe the challenges and the goals of biobank governance in the face of the transformative developments faced by contemporary biomedical research. The ultimate goal of such analysis and conceptualisation is to propose a revision of the ethical and legal normative framework applied to biobanks, starting from the assumption that the current framework is inadequate to protect research participants and society.

It is here, in my opinion, that the opportunity to study biobank governance from a bioethical perspective lies. The novelties that biomedical research and biobanks face today are unprecedented, as are the risks that individuals run in contributing their samples and personal data to a biobank, especially in terms of breaches of privacy, discrimination and other unwanted uses of their personal data. In turn, the contribution of bioethics is to fill the conceptual gap that is currently lacking to achieve updated and effective ethical and legal guidance.

Moreover, the specific case of biobank governance offers an interesting space for bioethical reflection, as it represents 'a prominent example of post-regulatory governance, involving complex, decentralized networks and mechanisms to ensure their alignment with participants' rights as well as with societal values and expectations'.[2]

Accordingly, the present work – intended as a conceptual analysis and redefinition of the problem of biobank governance – aims to provide insights and guidance for biobank stakeholders, understood as all those who have a role in regulating, designing, managing, using and participating in biobanks.

To date, there is no framework conceptualising biobank governance in the growing data-driven research and digital society. The scientific literature continues to discuss ethical, legal and social issues related to biobank activities within a normative framework intended for an analogue society and under the old paradigms of biomedical research ethics.

To fill this gap, this thesis aims to address the following research question:

What is an adequate model of biobank governance to foster biomedical research and innovation in a data-driven society while remaining aligned with societal values and expectations?

Throughout the dissertation, this question will be addressed with reference to three primary objectives:

- Following the Responsible Research and Innovation (RRI) framework embraced by the European Union, this dissertation pursues the objective of conceptualising a model of governance that provides a conceptual and practical structure for the

[2] F. Gille, E. Vayena and A. Blasimme, 'Future-proofing biobanks' governance' (2020) European Journal of Human Genetics 28.8: 989–996, p. 990.

implementation of ethical procedures aligned with the interests of research participants and society.

- The dissertation aims to identify and ethically analyse the specific challenges faced by biobanks in the light of the transformative developments brought by the digital paradigm to how biomedical research is conducted. Accordingly, a discussion of changing requirements in the understanding of the risks and opportunities in biobank participation is presented in order to design well-tailored goals for biobank governance.

- The dissertation aims to clarify the right principles to inform good governance of biobanks in data-driven biomedical research (transparency, data protection and participation), showing how they reflect the key challenges for biobanks and how they are well-suited to address the ethical, legal and social issues facing biobanks.

2. Methodology

At this point, a methodological clarification is required. The geographical perimeter of my research is Europe, for two reasons. Firstly, in recent decades, the phenomenon of biobanking has become widespread in this continent, especially in the light of national healthcare systems that facilitate the collection of biological materials, keep reliable health records and have a long-standing tradition of epidemiological research.[3]
The second reason concerns the specific circumstances of my doctoral journey in the last three years. The joint supervision agreement between the University of Bologna and the University of Barcelona allowed me to study in depth how the phenomenon of biobanking is regulated in two European counties, Italy and Spain, providing me with a good overview of the different approaches to the conceptualisation and regulation of biobanks in Europe, since the two countries rely on diametrically opposed approaches.

In addition, within the agreement between the two universities, I had the opportunity to observe closely the everyday practice, management and organisation of two biobanks: the

[3] K. Beier & C. Lenk, 'Biobanking strategies and regulative approaches in the EU: recent perspectives' (2015) Journal of Biorepository Science for Applied Medicine 3.1 69–81.

Italian BIObanca GENetica (BIOGEN)[4] – based at the Rizzoli Hospital of Bologna and part of the Telethon Network of Genetic Biobanks – and the Catalan IDIBAPS[5], based at the Hospital Clinic of Barcelona. I thus had an exceptional opportunity of studying the ethical, legal and social issues related to biobanking in theory and, simultaneously, to see how they are managed in practice and to discuss them with various biobank stakeholders. This has provided me with essential insights into the strengths and weaknesses of the current system of biobank governance.

Since my field of expertise is philosophy and bioethics, and the context in which I have conducted my research is highly interdisciplinary, the analysis that I have conducted in this dissertation integrates methodologies from diverse disciplines. Specifically, I have first conducted a review of the literature on the ethical, legal and social issues of biobanks, aimed at identifying the most authoritative arguments. Then, I have conducted an analysis of the ethical principles that inform the ethical and legal normative framework applied to biomedical research and biobanks, in order to compare them with the concrete challenges met in practice. Finally, case analyses are provided with the aim of showing the relevance of the ethical issues at stake.

3. Outline

This work unfolds in three consecutive stages: the definition of the pivotal concepts of bioethics, biomedical research, biobanks and governance that support the thesis; a critical analysis of the challenges faced by biobanks in the digital age in order to identify the priorities for an appropriate model of governance; and finally the proposal of a governance model with the presentation of a set of new ethical principles.

Accordingly, these stages are reflected in the distribution of the three central chapters. Chapter 1 addresses the previous questions, to lay the common ground against which to discuss the evolution of bioethics in the digital society, the inadequacy of the biomedical research ethics framework to provide appropriate guidance in the face of transformative developments in how biomedical research is conducted, the promising role of biobanks in

[4] https://www.ior.it/curarsi-al-rizzoli/biobanca-genetica-biogen
[5] http://www.clinicbiobanc.org/es_index.html

fostering research and innovation in data-driven biomedical research, and the understanding of biobank governance that permeates the dissertation.

Chapter 2 is devoted to a critical analysis of how the features of data-driven biomedical research may affect, influence and challenge biobanks today. The first challenge is identified in the fact that the digital paradigm as regards biomedical research implies new challenges for the traditional concepts of research ethics, in particular privacy and informed consent. These, in turn, render the traditional ethical framework inadequate to protect research participants. The second challenge regards the fact that data-driven biomedical research responds to a precise political, economic and societal commitment of the European Union towards a data-driven economy that, in the context of biobanks, is translated as a critical tendency towards the commodification of biobanks and associated data. A case analysis is presented to help understanding of the relevance of the ethical issues at stake.

Chapter 3 conceptually frames a broad vision of the phenomenon of the biobank and where the focus needs to be to move towards a societal and participatory model of biobank governance in a data-driven society. Accordingly, a model of biobank governance is presented, supported by an ethical framework comprising three principles – transparency, data protection and participation. The chapter ends with a discussion of how the proposed model is able to meet the need for an adequate ethical response to the challenges brought by the digital paradigm and how the principles are well-suited to enable biobank governance to achieve its goals.

Chapter 1
Previous questions

1. Introduction

In this chapter, I shall address previous questions related to the topic of this dissertation in order to pave the ground for future analysis. Accordingly, I will provide definitions of key concepts and questions before exploring the merit of conceptualising a governance model for biobanks in the digital society.

I believe that it is crucial to address the questions of what constitutes bioethics, biomedical research, a biobank and governance for two reasons. First, given that my research has been conducted in a highly interdisciplinary context – involving bioethicists, philosophers of law, data scientists, legal informatics and biomedical researchers – it is vital to establish a common background of definitions and understandings against which to discuss biobank governance, research ethics and data-driven biomedical research in the following chapters. Secondly, given the fact that the phenomena, challenges and issues addressed by this dissertation originate in the concomitance of substantial societal, ethical and scientific changes and the strong focus on future direction, I believe that it is important to set out the starting point of this journey and to visualise its end point in terms of bioethics, biomedical research and the role of biobanks in a digital society.

On the basis of these considerations, I will first clarify the account of bioethics that permeates this dissertation, in which it is seen not solely as a methodology but rather as an area of enquiry defined by its normative power to address the ethical challenges raised by the integration of biotechnologies and digital technologies in biomedical research. I will then describe what constitutes biomedical research, in its current configuration and future directions as a data-driven field. Accordingly, the role of research ethics committees is described as *trait d'union* between bioethics and biomedical research and an overview of the new demands of data-intensive research is provided.

At this point, I will describe in detail what biobanks are, how they are regulated in Europe, how they are organised and who the main stakeholders involved are. I will also clarify the promising role of biobanks in contemporary biomedical research. Finally, I will present an

overview of the origins of the concept of governance, its translation into the field of biomedical research and its application to biobanks. The chapter ends with a mission statement on what I believe is the most appropriate approach to biobank governance to meets the aims of my dissertation.

It is my intention that the existing questions addressed in this first chapter will serve as a map to enable familiarisation with the touching points, common challenges and shared issues in the fields of biomedical research, biobanks and research ethics together with a recognition of the need to bring together bioethics, biobanks and governance to face the challenges presented in the course of the dissertation.

2. What is bioethics?

Attempts to define bioethics and agreement on its status as a discipline have been persistent since the second half of the 20th century when the term made its first official appearance in the American scientific literature in Potter's *Bioethics: Bridge to the Future* (1971).[6] The history of the etymological origins of the term 'bioethics' and the dispute over its paternity is well-known and has become the subject of passionate debate.[7] Originally, the dispute was between two contenders: on the one hand, Potter, who understood bioethics as a bridge between biology and the humanities, highlighting the multidisciplinary nature of the discipline; on the other, the *Encyclopedia of Bioethics* issued in 1978 by the Kennedy Institute of Ethics of the University of Georgetown – one of the first academic centres dedicated to the study of bioethics – which described the new discipline as 'the systematic study of human conduct in the area of the sciences of life and healthcare, as this conduct is examined in the light of moral values and principles',[8] binding the discipline to medical ethics.

However, as argued by Baroni in *El origen de la bioética como problema*, assuming that the birth of bioethics as a discipline coincides with the history of the origins of its name is reductive for several reasons.[9] It can be argued, indeed, that bioethics existed long before it was given an official definition. The concept has existed under other names since ancient

[6] V.R, Potter,'Bioethics: Bridge to the Future' (Prentice Hall 1971); M. Casado & M. Lopéz Baroni, 'Manual de bioética laica (I). Cuestiones clave' (Edicions Universitat Barcelona 2018); M. Lopéz Baroni and others,'Manual de bioética laica (II). Cuestiones de salud y biotecnología' (Civitas Thomson Reuters 2021).
[7] W. T. Reich 'The word "bioethics": the struggle over its earliest meanings' (1995) Kennedy Institute of Ethics Journal, *5*(1), 19–34.
[8] W. T. Reich, *Encyclopaedia of bioethics* (Kennedy Institute of Ethics, University of Georgetown 1978).
[9] M. J. L. Baroni, *El Origen de la bioética como problema* (Vol. 7), (Edicions Universitat Barcelona 2016).

times, every time each society in any country established criteria to regulate the relationship between those who need care to heal and those who provide them with such care. Bioethics thus understood – argues Baroni – is part of the human heritage.
For this reason, the ongoing debate around the origins of the name and who first conceptualised the term risks conveying the idea that bioethics is solely a North American-related issue and fails to recognise adequately the multidisciplinary and transversal ways in which the concept has developed.

At the end of the last century, particularly during the 1980s and 1990s, amid a predominantly religious orientation (catholic and protestant), different secular, feminist and multicultural currents broke into the field of bioethics. Due to the nuanced conceptualisations and developments of bioethics, therefore, it is difficult to draw clear boundaries for bioethics as a field of enquiry. Unsurprisingly, the field of bioethics is today considered multidisciplinary and transversal, crossed by different experts (e.g. philosophers, legal experts, social scientists, politicians, medical professionals) and to which many disciplines (e.g. moral philosophy, human rights law, biomedicine, STS) can contribute.[10]

Based on these premises, it can rightly be said that bioethics is shaped in medical ethics as it received important input from the field of biomedicine in the West in the 1960s and 1970s and because, as observed by Dawson, with the beginning of the new century 'medical ethics has seemed an exciting area to work in because of the constant technological innovations in medicine, and the dramatic life and death issues that often lie at its heart'.[11]

However, it can also be argued that bioethics as an inner social and global vocation – which interestingly was the line pursued by Potter[12] in the early 1970s and is now very popular among contemporary bioethicists – releases the understanding of bioethics from its dependence on medical ethics. I am talking here of an account of bioethics that is oriented to reflect on the ethical issues that affect us as a community, beyond the focus on the individual that is typical of medical ethics and, also, beyond a focus on human beings,

[10] J. Montgomery, 'Bioethics as a governance practice' (2016) Health Care Analysis, *24*(1), 3–23.
[11] A. Dawson, (2010). 'The future of bioethics: three dogmas and a cup of hemlock' Bioethics, *24*(5), 218–225.
[12] V. R. Potter, *Global bioethics: building on the Leopold legacy* (MSU Press 2012).

including in its scope other living beings, the environment, and the challenges of the globalised world.[13]

An outstanding example of this understanding of bioethics is found in the response given by the British bioethicist John Harris to the question 'What is bioethics?':

> [It] is literally the ethics of our interaction with the biosphere and covers everything from individual ethical dilemmas 'should I eat meat?', 'would I be wrong to terminate my pregnancy?' to questions concerning the ethics of the improvement of global health and global justice both between generations and within them, in enhancing the lives of groups and individuals, rich and poor, in sickness or in health, and in respect of all conceivable powers and capacities, including intelligence, physical, artistic and sporting prowess, and not excluding changes so radical they might lead to the further evolution of our species up to and beyond a point at which we would judge a new successor species to have been created.[14]

In general, bioethics in the 21st century recognises the global scope of problems and the global nature of required solutions. This is in line with the global dimension implicated in Potter's work, which was the understanding that the fundamental problems with which bioethics is concerned, such as population growth and poverty, affect all humankind and, therefore, bioethics' goal of survival is global, since what is at stake is the survival of humanity. This, in turn, concerns health care, the biosphere, future generations and social justice.[15]

In more concrete and contemporary terms, it can be argued that global bioethics is:

> the study of global ethical problems related to health, healthcare, health science and research, and health technologies and policies, and the activities, practices and policies to influence and resolve these global problems.[16]

[13] I. de Lecuona Ramírez, *Los comités de ética como mecanismos de protección de los derechos humanos en investigación biomédica* (Doctoral dissertation, Universitat de Barcelona 2011).
[14] J. Coggon, S. Chan, S. Holm, & T. Kushner, (Eds.) *From reason to practice in bioethics: An anthology dedicated to the works of John Harris* (Manchester University Press 2015).
[15] H. A. Ten Have, 'Potter's notion of bioethics' (2012) Kennedy Institute of Ethics Journal, *22*(1), 59–82.
[16] H. Ten Have, *Global bioethics: An introduction* (Routledge 2016) 243

Accordingly, as argued by Hellsten, global bioethics today concerns global health issues and global distributive justice in the name of 'an increasing awareness of the interrelatedness of peoples and their ethical dilemmas, and the recognition that global problems need global solutions'.[17]

Despite these unquestionable premises regarding the transversal, global and evolving nature of bioethics that severely complicate the task of defining bioethics, I shall – for the sake of the interdisciplinary academic environment of this dissertation – clarify and narrow the understanding of bioethics that I propose in this dissertation and, in particular, the way I conceive the scope, methodology and approach that form its basis.

In doing so, I am aware that I am taking a stand and choosing a specific perspective from which to approach the topics and issues of this work while other equally valid perspectives may exist. Accordingly, in what follows I shall explain and justify the perspective from which I have decided to shape my understanding of bioethics and the theoretical proposal that I aim to advance in this work.

Starting from the epistemological question on the status of bioethics as a field of enquiry, I rely in this dissertation on a specific definition of bioethics as that field of enquiry that critically reflects on the ethical challenges caused by the impact of biomedical research – as well as technological and digital advances – on human beings.

This account of bioethics is informed by the debate on the future of bioethics which has taken place over the last decade.[18] Accordingly, I maintain that an overlap between bioethics and medical ethics is too reductive, especially concerning the objects of study and the ethical principles involved. Such a narrow vision has indeed started to show its inadequacy with the emergence of new and unique contemporary ethical challenges brought by the advance of biotechnology and the digital society.

The principal problem of a narrow vision of bioethics, reduced to medical ethics, is the tendency to consider certain 'dogmas' at the basis of medical ethics as universal truths. For instance, as noted by Dowson, we witness in bioethics 'the ubiquity of the assumption about

[17] S. K. Hellsten, 'Global bioethics: utopia or reality?' (2008) Developing World Bioethics, *8*(2), 70–81.

[18] Dawson, Three dogmas; R. Macklin, 'The death of bioethics (as we once knew it)' (2010) Bioethics, *24*(5), 211–217; S. Sherwin, 'Looking backwards, looking forward: hopes for bioethics' next twenty-five years' (2011) Bioethics, *25*(2), 75–82.

the importance of autonomy',[19] which is seen as the most important moral value or principle. This dogma is likely to prevent bioethical analysis and discussion from providing a valuable guide for the ethical challenges raised in the context of data-intensive biomedical research that requires updated ethical guidance.

In contrast, in this dissertation, I advocate for a bioethics that narrows its focus to the ethical challenges related to biomedical research in order to provide the ethical counterpart of an critical conscience for the technological and digital advances of this century, understanding the challenges of their global scope.

I suggest a bioethics based on philosophy that is broader than medical ethics and committed to overcome the recognised deadlocks and dogmas of the traditional medical ethics paradigm – primarily, the principle of autonomy and informed consent – that fail to provide adequate ethical guidance to navigate the challenges brought by the digital society and data-driven biomedical research. In this sense, the contribution of philosophy to bioethical reflection is essential in understanding the new context and discussing contemporary bioethical issues. Indeed, as provocatively observed by Savulescu, we should move away from medical ethics as 'philosophical thinking is the most important activity in medicine and in life—ethics determines what we should do. Science can only tell us how to do it' .[20]

Secondly, regarding its global vocation, I propose an account of bioethics bound by human rights and understood as shared and internationally recognised common ethical-legal standards.[21] I refer in particular to the UNESCO Universal Declaration on Bioethics and Human Rights,[22] approved by the 33rd UNESCO General Conference in 2005, that binds signature States to a set of common principles on ethical issues related to medicine, life sciences and technologies applied to human beings. The Declaration has the recognised merit of being a useful framework for addressing global issues and, at the same time,

[19] Dawson, (n 6) Three dogmas.

[20] J. Savulescu, 'Bioethics: why philosophy is essential for progress' (2015) Journal of Medical Ethics, *41*(1), 28–33.

[21] G. Solinís (2015) *Global Bioethics: What for? 20th anniversary of UNESCO's Bioethics Programme* (UNESCO Publishing).

[22] UNESCO (2005) *Universal Declaration on Bioethics and Human Rights,* https://unesdoc.unesco.org/ark:/48223/pf0000146180 Accessed 20 March 2022.

definitively links bioethics – as a discipline and a common framework for reaching an agreement – with internationally recognised human rights.[23, 24]

The principles put forward are respect for human dignity, autonomy and social responsibility, consent, respect for human vulnerability and personal integrity, privacy and confidentiality, equality, justice and equity, non-discrimination and stigmatisation, respect for cultural diversity and pluralism, solidarity and cooperation, social responsibility and health, benefit-sharing, the protection of future generations and preservation of the environment, the biosphere and diversity. This brief overview allows us to see that the Declaration is committed to the protection of the person, from the individual level to a collective level that includes future generations and the entire environment.

Accordingly, I maintain that the human rights framework outlined by the UNESCO Declaration on human rights and bioethics represents the context for bioethical reasoning in the West and the starting point for future approaches to the ethics of biomedical research, based on the assumption that bioethical principles and human rights inform one another.[25]

Finally, I defend an account of bioethics that fits into the current trend of research governance pursued by the European Union in the context of the Responsible Research and Innovation framework, and that sees ethics as a responsibility shared between the various stakeholders involved in scientific progress.[26] Such an approach becomes imperative in a context like that of biomedical research, where asymmetric relationships and ethically inadequate practices may easily occur. Accordingly, approaching ethical discussion and analysis from the perspective of governance – understood as a combination of formal and informal norms, processes, documents and behaviours – seems to be the correct way to shed light on a complex system created by different stakeholders with different interests and expectations. As argued by Montgomery, the former Chair of the prestigious Nuffield Council of Bioethics, we should shift the focus of the practice of bioethics from an intellectual enterprise to a governance one, 'studying bioethics as a governance practice focuses more

[23] H. Ten Have 'The Universal Declaration on Bioethics and Human Rights as a landmark in the development of global bioethics', in *International Biolaw and Shared Ethical Principles* (Routledge 2018) 31–39); Casado, M. (coord.) (2009). *Sobre la dignidad y los principios: análisis de la Declaración sobre bioética yderechos humanos de la UNESCO* (Navarra: Civitas) 441-451.

[24] I. de Lecuona Ramirez (2009). «Los comités de ética como mecanismos de aplicación de la Declaración Universal sobre bioética y derechos humanos de la UNESCO (art. 19)» In Casado, *Dignidad y Principios.*

[25] I. de Lecuona, *Los comités de ética* (2011).

[26] European Commission, Directorate-General for Research and Innovation, (2014) *Responsible research and innovation: Europe's ability to respond to societal challenges* (Publications Office).

on *who* does things, *how* and *why* they do them, than in what they study and what they conclude'.[27]

Following this line of reasoning, I do not claim that a practical approach should supersede my previous understanding of bioethics as a conceptual analysis based on philosophy; rather, I believe that approaching bioethics also as a governance practice is complementary. In particular, it stresses the importance of translating principles into practice and implementing concrete instruments of bioethics oversight, such as committees and guidelines.

I shall now clarify the objective of the account of bioethics that I have presented so far and its expected contribution to this dissertation. Starting from the objective, I believe that – compared to other approaches – the philosophical approach and method should ensure that the bioethical analysis and assessment of a specific issue will always be the outcome of critical reasoning (in the Socratic questioning spirit) rather than a repetition of truths assumed to be unquestionable in the context of biomedical research (e.g. 'we must respect patient autonomy, so we need to obtain informed consent'). This is because, as argued by Dawson, the philosophical approach allows us:

> to keep asking questions about the fundamental aspects of what is happening and what ought to happen, identifying and discussing fundamental values, analysing and exploring the meaning of concepts, and asking questions about consistency and the power of arguments more generally.[28]

Secondly, I hold that the principal contribution of this understanding of bioethics to the topic of this dissertation – namely, the conceptualisation of a governance model of biobanks in the digital society – is the normative power of its conceptual analysis. As brilliantly argued by Camporesi and Cavaliere:

> bioethics requires specific training in critical thinking and moral philosophy to reason through the complex normative questions raised by biotechnologies, biomedicine and the life sciences. While ethical oversight is not, nor should it be, the realm only of

[27] J. Montgomery, 'Bioethics as a governance practice', (2016) Health Care Analysis, *24*(1), 3–23.
[28] Dawson, (n 6) Three dogmas.

bioethicists, we argue that bioethicists are at an epistemic advantage when reasoning over bioethical questions.[29]

It is precisely this epistemic advantage, or authority, recognised in an account of bioethics based on philosophy, that I hope will allow this dissertation to meaningfully contribute to the normative discussion on ethical issues raised by biomedicine and technology.

To conclude, for the purposes of the remainder of this work, this definition of bioethics will be adopted as the scope of the analysis and as a starting point for the conceptualisation of a governance model for biobanks in the digital society – that is, a continuous conceptual analysis and clarification of issues, arguments and principles related to the ethical challenges raised by biotechnological and digital advances to biomedical research, and their implications for biobank governance. This analysis should always be driven by a Socratic questioning spirit that allows us to look beyond the assumptions and dogma of medical ethics and the traditional hierarchy of values and principles, on the basis of the recognition of ethical pluralism – the recognition that many relevant values need to be weighed and balanced against each other.

Nevertheless, I cannot ignore that bioethics is fundamentally interdisciplinary and multidisciplinary. I am aware of the importance of the contribution of social sciences[30] and empirical approaches[31] to bioethics, and also of the strong ties that bind bioethics to the legal domain.[32] Although the aforementioned approaches lie beyond my expertise and background, I strongly believe that only a joint effort can achieve a governance scenario for technoscience and the digital society that is ethical and aligned with societal values and expectations. In this sense, I hope that the conceptual analysis that I will conduct in this dissertation could serve as a starting point for a further multidisciplinary study.

In addition, it is important to take into account that this dissertation is also committed to following the evolution of bioethics in the digital society. While the previous bioethics era

[29] S. Camporesi & G. Cavaliere, 'Can bioethics be an honest way of making a living? A reflection on normativity, governance and expertise' (2021) Journal of Medical Ethics, *47*(3), 159–163.
[30] M. Schneider, E, Vayena & A. Blasimme, 'Digital bioethics: introducing new methods for the study of bioethical issues' (2021) Journal of Medical Ethics; G. Pavarini and others, 'Design bioethics: A theoretical framework and argument for innovation in bioethics research' (2021) The American Journal of Bioethics, *21*(6), 37–50.
[31] J. E. Pacyna & R. R. Sharp, 'The Need for "Big Bioethics" Research' (2022) The American Journal of Bioethics, *22*(1), 3–5.
[32] M. Casado, 'Bioética y Derecho', in H. Gros, Y. Gómez 'La Declaración Universal sobre Bioetica y Derechos Humano de la UNESCO'(pp.29-46) (Comares, Granada 2006)

(the past two decades) has seen bioethicists struggling with serious ethical challenges, such as the regulation of gene editing on human beings and other epochal innovations derived from the application of biotechnology to human beings, the new era has to address the adoption and integration of Information and Communication Technologies (ICT) into the field of biomedical research, and the ethical implications raised by the 'datafication' of our health. It can be argued that this informational turn in our society has given way to a new era of bioethical discussion that could be called 'bio-data-gen-ethics', a combination of biotechnology and ICT that gives rise to an unprecedented and challenging phenomenon in the use of biotechnology to extract data from an individual's biological samples and exploit those personal and sensitive data for various purposes. Therefore, bioethics is called on today to fill the conceptual deficit that commonly arises when facing new and unprecedented challenges.

2.1. Ethics of biomedical research

In order to progress to the next chapters with a comprehensive common understanding of the state of the art regarding ethical framework applied to biomedical research and biobanks, I shall now briefly identify and analyse the international ethical-legal instruments that have allowed the opening and consolidation of bioethics reflection in the international sphere, with consequent impact on states through the development of regulations, policies and actions.

I refer to the most relevant texts, documents and guidelines of bioethics that constituted the basis for medical ethics, health care ethics, biomedical research ethics and research ethics[33] during the 20th century[34]: the Belmont Report (1979)[35], the WMA Declaration of Helsinki on Ethical Principles for Medical Research Involving Human Subjects, Helsinki, Finland, 1964

[33] The terms 'medical ethics', 'health care ethics', 'biomedical research ethics' and 'research ethics' are often used interchangeably. While they have many points in common, it is important to note that they refer to different practices. For the purposes of this dissertation, I refer only to research ethics and biomedical research ethics (using these terms interchangeably), which I understand specifically as the normative framework and set of principles that provide ethical guidance on all practices involving biomedical research with human participants or with human biological samples and associated data.

[34] It is important to acknowledge here the Nuremberg Code which can be considered the precedent of any attempt to normalise the ethics of medicine and biomedical research. The Code was issued in 1946 as a result of the Nuremberg trials held at the end of World War II.

[35] The Belmont report: ethical principles and guidelines for the protection of human subjects of research (1979). National Commission for the protection of human subjects of biomedical and behavioural research. Available at: https://www.hhs.gov/ohrp/regulations-and-policy/belmont-report/read-the-belmont-report/index.html Accessed 10 March 2022.

(last revision 2013)[36], the European Convention on Human Rights and Biomedicine usually referred as Oviedo Convention (1997),[37] the Charter of Fundamental Rights of the European Union (2000)[38] and the UNESCO Universal Declaration on Bioethics and Human Rights (2005).[39]

Taken together, they make a substantial contribution to addressing the ethical issues related to medicine, biomedical research and associated technologies as applied to human beings. They also provide a universal framework of bioethical principles and procedures to guide States in the formulation of their legislation, policies and practice in the field of biomedical research and biotechnologies, aiming to avoid misuse and protect the rights of those human beings involved. The rights and fundamental freedoms of research participants that these documents aim to respect and protect – and that constitute the value system underlying all bioethical principles – are the right to life and dignity, the right to integrity (physical and moral), the right to self-determination, the right to privacy and confidentiality of personal information and the right not to be discriminated against for medical and genetic reasons.

By way of illustration, I shall examine the Belmont report and the Oviedo Convention. The former was published in 1979 as the result of a commission to identify the ethical principles that should govern scientific research on human beings, instigated by the US government for the protection of human subjects in scientific and behavioural research. These principles are those of respect of persons, beneficence and justice.

This normative framework was subsequently extended by two of the authors of the Belmont report – Beauchamp and Childress – who in 1994 published the book *Principles of Biomedical Ethics.*[40] It presents what has become one of the most applied bioethical frameworks in the fields of biomedical research, medicine and public health, known as 'the four principles approach'.

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[36] World Medical Association. 'World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects' (27 Nov 2013). Available at: https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/ Accessed 10 March 2022.

[37] Council of Europe, Convention on Human Rights and Biomedicine (Oviedo Convention) (ETS No 164). Available at https://www.coe.int/en/web/conventions/fulllist?module=treaty-detail&treatynum=164 Accessed 10 March 2022.

[38] European Union: Council of the European Union, 'Charter of Fundamental Rights of the European Union' *(2007/C 303/01)*, 14 December 2007, C 303/1. Available at: https://www.refworld.org/docid/50ed4f582.html. Accessed 10 March 2022.

[39] UNESCO 'Universal Declaration on Bioethics and Human Rights', 19 October 2005. Available at: https://unesdoc.unesco.org/ark:/48223/pf0000146180. Accessed 10 March 2022.

[40] T. L. Beauchamp, & J. F. Childress (1994). *Principles of biomedical ethics*. Edicoes Loyola.

The principles on which the decision-making processes, procedures and practices involving humans should be based are respect for autonomy, beneficence, no maleficence, and justice. Translated into practice, the principle of autonomy ensures adequate information, understanding and voluntariness for individuals involved in biomedical research through informed consent procedures. The principles of beneficence and no maleficence refer to the need for decisions and actions in this context to be pursued with the aim of maximising benefits and minimising risks. Finally, the principle of justice concerns, on the one hand, the importance of a fair selection of participants in research and respect for their right not to be discriminated against for genetic or medical reasons and, on the other, equal access to research and the equal distribution of benefits and burdens.

The Oviedo Convention issued by the Council of Europe represents the first binding legal text – for those Member States that have ratified it – to address the protection of the fundamental rights of human beings with regard to the applications of medicine and biology for present and future generations at international level.[41] It is considered a fundamental point of reference for bioethics as it establishes for the first time the need to foster social debate on the issues and challenges raised by advances in biomedical research and biotechnologies and their applications for human beings. This debate needs to take into account ethical, legal and societal implications as a preliminary step in political decision-making. Furthermore, the Oviedo Convention recognises that protection against the threat posed by unregulated use of bio-techno-scientific progress on human beings should be established at several levels: individual, social and as a species. Accordingly, the principles promoted are based on the recognition of dignity and identity as essential human values to be respected and assured, so that the interests of science and society never prevail over them, and at the same time on equitable access to health and research benefits with the prohibition of unjustified discrimination.

It is against this framework that this dissertation discusses an effective model of biobank governance for the digital society. In particular, the principle of autonomy, the prohibition of financial gain and disposal of human body parts, and the principles of respect for participants' privacy and confidentiality of personal information will be analysed and critically

[41] M. L. Marín Castán (2021) 'Sobre el significado y alcance de los hitos más decisivos en el desarrollo de la bioética universal: el Convenio de Oviedo y la Declaración Universal sobre Bioética y Derechos Humanos de la UNESCO' *Revista de Bioética y Derecho*, (52), 155-172; M. Casado & M. J. López Baroni (2021) *El Convenio de Oviedo cumple veinte años: propuestas para su modificación* (Edicions de la Universitat de Barcelona).

discussed in the light of the new risks and challenges that the digital paradigm has brought to biomedical research and biobanks. Furthermore, two main applications of this traditional ethical framework will be critically assessed: informed consent and research ethics committees. Informed consent – probably the most discussed topic of biomedical research ethics[42] – is the ethical tool and legal basis that ensures the respect of individual autonomy of participants involved in any medical procedure and biomedical research concerning the individual itself and/or her biological samples and associated personal data. Research ethics committees are the overview tool that ensures the protection of the human rights of the individuals involved in biomedical research and, at the same time, that scientific interests never prevail over those of individuals. This dissertation will question the role and scope of informed consent and ethical overview systems in the field of biobanks.

2.2. Bioethics for the digital society

If at a micro level, this traditional ethical framework for biomedical research is challenged in the remainder of this work with the goal of proposing new ethical principles for biobank governance in a data-driven biomedical research context, this goal reflects on a macro level the effort to rethink bioethics for the digital society.

Indeed, according to the annual horizon-scanning undertaken by the Nuffield Council on Bioethics[43] to investigate ethical issues related to advances in biology and medicine, it appears clear that the majority of critical ethical challenges today are related to the adoption and integration of Information and Communication Technologies (ICTs) in most aspects of our lives – in other words, the arrival of the digital society. Indeed, digital innovations and infrastructures are reshaping our society, economy, education, health and recreation at a scale and speed as never before. The combination of mobile and cloud technologies, big data, Artificial Intelligence, algorithms and the Internet of Things offers unimaginable

[42] N. Manson, O. O'Neill, 'Rethinking informed consent in bioethics' (Cambridge University Press 2007); T. Beauchamp, 'Informed Consent: Its History, Meaning, and Present Challenges' (2011) Cambridge Quarterly of Ethics 20(4), 515-523; C. Grady, 'Enduring and emerging challenges of informed consent' (2015) New England Journal of Medicine 372 (9). 855-862.

[43] An independent body based in London that examines and advises on ethical issues arising from biomedicine and health. Founded in 1991, it has achieved an international reputation for advising policy makers and stimulating public debate in bioethics. See https://www.nuffieldfoundation.org/research/nuffield-council-on-bioethics Accessed 4 October 2021

opportunities, driving growth, improvements in people's lives and efficiency in many areas, including medicine and health services.

Unsurprisingly, in the new report issued by the Nuffield Council on Bioethics in January 2022, the issue of 'health data and research' within the cluster 'data and technology'[44] appears for the first time. Thus, today bioethics is called into action to face the challenges brought by the increasing volume of health-related personal data collected and shared in the clinical setting, by biobanks but also through smartphones and wearables. The primary challenge is highlighted in the Nuffield Council's report that claims:

> There is a high economic and political interest in the potential of health data to advance scientific research and bring benefits to patients. Those governing and designing data initiatives find themselves in a situation where they are obliged to generate, use and extend access to data, while at the same time protecting individual private interests.

As we will explore in the following chapters, in a digital society, bioethics should be committed to understanding and clarifying the ethical implications of this new digital asset in biomedical research in terms of both opportunities and risks, eventually providing theoretical guidance for the pursuit of ethical procedures. We will see that data-driven biomedical research raises many novel ethical challenges, related primarily to the fact that biomedical datasets can be aggregated and re-purposed, generating unprecedented concerns related to informed consent, ethical overview, privacy, confidentiality and data protection.[45]

3. What is biomedical research?

I shall now offer a definition of biomedical research since it represents the main field, together with that of biobanks, in which my bioethical enquiry will evolve throughout this dissertation.

In the most general terms, biomedical research is a specific sector of scientific research. According to the International Ethical Guidelines for Biomedical Research Involving Human

[44] https://www.nuffieldbioethics.org/what-we-do/horizon-scanning
[45] B. D. Mittelstadt & L. Floridi (Eds.) *The ethics of biomedical big data,* Vol. 29 (Springer 2016).

Beings Prepared by the Council for International Organisations of Medical Sciences (CIOMS) in collaboration with the World Health Organization (WHO) issued in 2002, scientific research is:

> A class of activity designed to develop or contribute to generalisable knowledge. Generalisable knowledge consists of theories, principles or relationships, or the accumulation of information on which they are based, that can be corroborated by accepted scientific methods of observation and inference.[46]

Adding the adjective 'biomedical' to the term 'research' narrows the field of enquiry to those scientific research activities related to the health of human being, usually using biotechnological techniques. More specifically, a first definition of biomedical research could be that area of science devoted to the study of the processes of life, the prevention and treatment of disease, and the genetic and environmental factors related to disease and health.

However, to better delimit the scope of biomedical research is difficult, since it is an evolutionary process that involves many levels, each of which belongs to a different and specific scientific discipline. This complexity is recognised in the definition of Flier and Loscalzo, which refers to biomedical research as:

> A subset of research [that] is broad in scope, referring to activities spanning many disciplines of biology and medicine. Within these broad disciplines are experiments designed to understand reality by examining events at many different levels of organisation, from the atomic level (e.g., structure of key biologic molecules), to the molecular and cellular levels (e.g., biochemistry, cell biology), to the organismal level (e.g., physiology and pathophysiology), and to the population level as well (e.g., population genetics, epidemiology, and public health).[47]

From this definition, we can infer the subcategories into which biomedical research is usually divided: basic, clinical and epidemiologic research. To these 'traditional' categories, we must

[46] Council for International Organizations of Medical Sciences, 'International ethical guidelines for biomedical research involving human subjects' (2002) Bulletin of medical ethics (182), 17–23.

[47] J. S. Flier & J. Loscalzo, 'Categorizing biomedical research: the basics of translation' (2017) The FASEB Journal, *31*(8), 3210–3215.

add a new one that indicates the future direction of biomedical research: translational research.

Basic research is conducted to increase the knowledge base and, in particular, the physical, chemical and functional understanding of the mechanisms of life processes and diseases. Clinical research consists in using the knowledge gained in basic research to conduct research, generally with humans in a hospital or clinical setting, concerning the manifestation, diagnosis and treatment of diseases. Epidemiologic research investigates the risk factors of diseases, their frequency and their impact on the population and public health.

Finally, translational research is 'an interdisciplinary branch of biomedical science supported by three main pillars: bench side, bedside and community'.[48] It can be inferred that translational biomedical research represents the culmination and a new direction for all the activities described above, as it is committed to the process of applying the discoveries made during basic and clinical research to the development of trials and studies with patients and participants. Equally, it is concerned with translating results on best practice to the community, for example, in prevention and treatment strategies.

On the basis of this overview, I shall now highlight three features of biomedical research that are key for the purpose of this dissertation. First, this work is interested in biomedical research as it involves health-related research with humans, including research with human biological samples and health-related data. Secondly, it is important to note that the main objective of biomedical research is the development or the enhancement of knowledge and not any direct benefit to the health of an individual patient or participant. Finally, for these inherent features, and to be truly beneficial for society, it is fundamental that biomedical research be subjected to continuous assessment, control and follow-up from ethical, legal and social perspectives.

To conclude, I would like to note that, while biomedical research is a relevant context for this dissertation, the true focus of the following chapters will be the move towards data-driven research and personalised medicine. Specifically, it is worth emphasising that this dissertation is committed to tackling the ethical implications of how biomedical research is conceived and carried out today and, in particular, its impact on biobank governance.

[48] R. J. Cohrs, 'Translational medicine definition by the European society for translational medicine' (2015) New Horiz. Transl. Med. 2, 86–88.

The new direction, as elaborated below, is characterised by two features. First, a change of paradigm has been claimed by many scholars:[49] taking advantage of digital technologies and exploiting 'omics' data, biomedical research is increasingly figuring as a process of the accumulation of data and sharing of evidence on a large scale and across research contexts as a starting point for the research process. From here, the use of the term 'data-driven' biomedical research is justified.

Secondly, the main consequence of this focus on data collection and sharing is a massive effort in building infrastructures such as databases and biobanks for the dissemination of data across research centres.[50]

3.1. Data-driven biomedical research

In the continuation of this work, the term 'biomedical research' will be preceded by the adjective 'data-driven', because data-driven biomedical research is the way in which most biomedical research is conducted today. In this paragraph, I shall give a simple definition of this phenomenon as a fundamental requirement for later applying an ethical reflection. In the Encyclopedia of System Biology, Leonelli defined data-intensive research thus:

> Data-intensive research can be characterised as the attempt to extract biological knowledge from the huge amounts of data produced through experiments and high-throughput technologies (e.g., new generation DNA sequencing) and disseminated through cyberinfrastructures (e.g., community databases and Bio-Ontologies).[51]

This phenomenon fits into a broader revolution, currently characterised in the scientific literature in multiple fields as 'big data'.

[49] T. Hey and others (Eds.) *The fourth paradigm: data-intensive scientific discovery* (Redmond, WA: Microsoft Research 2009).
[50] S. Leonelli, 'Introduction: Making sense of data-driven research in the biological and biomedical sciences' (2012) *Studies in History and Philosophy of Science Part C: Studies in History and Philosophy of Biological and Biomedical Sciences*, *43*(1).
[51] S. Leonelli 'Data-Intensive Research' in W. Dubitzky and others (eds.) *Encyclopedia of Systems Biology* (Springer 2013) 545.

Many attempts have been made to find a comprehensive definition of big data in the literature, but a lack of consensus prevails.[52] The task is particularly difficult because it tries to capture a phenomenon in motion and evolution. The most straightforward characterisation of big data in the literature that we can assume as a basic tenet defines it as large data sets produced in a digital form that can be analysed through computational tools that perform data analytics and data mining. These datasets are usually described by their main features, commonly known as the '3Vs': huge in Volume, diverse in Variety and high in Velocity.[53] However, it seems that the number of 'Vs' is increasing over time, now reaching ten, including variability, veracity, visualisation and value).[54]

Although most of the above features refer to big data's physical attributes, for the sake of my argument, it is worth emphasising the importance of 'value', among other features, that is, defining data by virtue of what can and cannot be done with them or, in other words, how we can exploit them. Indeed, the reference to big data's physical attributes, and even the adjective 'big', simply describes this phenomenon in terms of a huge and complex system that our computational tools struggle to manage in comparison to what existed previously. However, since my research takes a bioethical perspective, it is interesting to note that by approaching big data for their value, the possibility is raised of an ethical analysis of data-driven biomedical research.

Going back to data-driven biomedical research, I shall first clarify the true innovative scope of the use of big data in biomedical research. Indeed, the importance of data in this sector is not new: biomedical research – and particularly the fields of genetics, epidemiology and pharmacology – has an extensive tradition of tackling massive data sets. Thus, the innovation lies in two factors: the first is the advancement of Information Technologies (IT) and, in particular, bioinformatics technologies that provide adequate 'data repositories, computing infrastructures, and efficient data manipulation tools for investigators to gather and analyse biological information';[55] the second one lies in the phenomenon of the convergence of technologies that is a typical feature of the digital society. That is the process

[52] R. Kitchin, *The Data Revolution: Big Data, Open Data, Data Infrastructures & Their Consequences* (Sage 2013); R. Kitchin, 'Big data and human geography: Opportunities, challenges and risks' (2013) Dialogues in Human Geography 3(3): 262–267.
[53] C.L. Philip Chen & C.Y. Zhang, 'Data-intensive applications, challenges, techniques and technologies: a survey on Big Data' (2014) Information Sciences 275: 314–47.
[54] M. Drosou and others, 'Diversity in big data: a review' (2017) Big Data 5(2):73–84.
[55] N. H. Shah & J. D. Tenenbaum, 'Focus on translational bioinformatics: The coming age of data-driven medicine: translational bioinformatics' next frontier' (2012) Journal of the American Medical Informatics Association: JAMIA, *19*(e1), e2.

by which existing technologies merge into new forms of technologies with unprecedent potential and innovative power[56]. In the field of biomedical research, a prominent example is the convergence between synthetic biology and Artificial Intelligence that in the field of genomics research continue to expand the use of computational methods such as artificial intelligence and machine learning to improve the understanding of hidden patterns in large genomics datasets coming from basic and clinal research contexts[57]. Thus, the boundaries between biotechnology, synthetic biology, nanotechnology and Artificial Intelligence have disappears and in order to feed the resulting new technologies, a massive accumulation of biological and clinical data is required. to be generated and collected at an unprecedented speed and scale.

Together, those two factors allow big data to be defined as 'datasets whose size is beyond the ability of typical database software tools to capture, store, manage, and analyze'[58] and 'characterized by being generated continuously, seeking to be exhaustive and fine-grained in scope, and flexible and scalable in its production'.[59]

Today, biomedical research is particularly affected by the rise of big data, with prominent examples found in genomic sequencing and the wider range of omics research. It can be argued that we are experiencing a flood of genomic data, destined to expand further. In this regard, Cohen and colleagues reported in 2018:

> Due to the falling costs of genomic sequencing and an emphasis on genomic data for clinical and research applications, it is estimated that by 2025, between 100 million and 1 billion human genomes will be sequenced, pushing data generation into the exabyte (one billion gigabyte) scale. Advances in bioinformatics and analytics are leveraging personal data to further health and biomedical knowledge and applications. New machine learning techniques, for instance, are now being used to analyze Big Data and help doctors provide diagnosis and treatment to patients.[60]

[56] M. Baroni, 'Bioética y tecnologías distruptivas' (Herder Editorial 2021).
[57] A. Shmulewitz and others, 'Convergence in biomedical technology' (2006) Nature Biotechnology 24 (3) 277-277.
R. Dias & A. Torkamani, 'Artificial intelligence in clinical and genomic diagnostics' (2019) Genome medicine, 11 (1) 1-12.
[58] J. Manyika and others, *Big data: the next frontier for innovation, competition, and productivity*, (McKinsey, 2011). http://www.mckinsey.com/business-functions/business-technology/our-insights/big-data-thenext-frontier-for-innovation Accessed 1 March 2022.
[59] R. Kitchin, 'Big Data, new epistemologies and paradigm shifts' (2014) Big Data & Society, *1*(1).
[60] I. Cohen and others, (Eds.) *Big data, health law, and bioethics* (Cambridge University Press 2018) 2.

In the face of this phenomenon, understanding how big data are defined and identified in biomedical research is the first fundamental step. The kind of information[61] we refer to when we talk about biomedical big data is biological information derived from the analysis of a range of physical or biological characteristics of a person.

The best-known example of biological information is the genetic and heritable biological information coded in a sequence of DNA. In an introduction to the concept of information, Floridi argues that, from a linguistical perspective, the adjective 'biological' matched with 'information' can have an attributive use (biological information is information about biological facts) or a predicative use (biological information is information whose nature itself is biological).[62] While the attributive sense of biological information is common and easy to understand (e.g. a database that contains medical and genetic information about a group of patients), understanding the predicative sense is more complex, yet crucial for our aim in this paragraph. Biological processes and elements are intrinsically informational in themselves. Taking as a reference genetic information, and following Floridi's reasoning:

> DNA contains the genetic code, precisely in the sense that it physically contains the genes which code for the development of the phenotypes. So, DNA does contain genetic information, like a CD contains some software. But the genetic code or, better, the genes, are the information itself.[63]

Therefore, biological information in the predicative sense of the term is procedural: it is information for something. Bearing in mind this double characterisation of biomedical data as both biological information *about* something and information *for* something, we can move to the question of what constitutes biomedical big data as a supply source for data-driven biomedical research.

Valuable biomedical big data can exist in many forms and come from various fields. They are usually clinical care data, laboratory data, genomic sequencing data or data from various other fields of biology ending in -omics (e.g. proteomics, metabolomics, microbiomics).[64] We

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[61] W. Lawrence, *Privacy, confidentiality, and health research* Vol. 20, (Cambridge University Press 2012) In accordance with Lawrence, I understand the relationship between data and information in the biomedical context to be as follows: data are records of observations or facts (i.e. raw numbers, graph, images, digital bites handled in a digital form. Information is a data set with an interpretative context to generate meaning. Therefore, raw data mean nothing without an interpretative concept, and, at the same time, information depends on data.

[62] L. Floridi, *Information: a very short introduction* (Oxford University Press 2010).

[63] Ivi, p. 79.

[64] Nuffield Council on Bioethics, The collection, linking and use of data in biomedical research

can group them according to their origins: i) aggregated clinical trial data; ii) genetic and genomics sequencing data; iii) biological specimens; iv) electronic health records and administrative hospital data.[65] Such data can be held in biobanks, cyberbanks or virtual research repositories that are designed to assemble aggregated datasets explicitly for research.

Another way to classify and understand big data in biomedical research, following Vayena's proposal, is to distinguish between biomedical big data and non-biomedical big data with high biomedical value. The latter are health-related information collected and/or shared through loyalty cards points, social media and mobile devices from which they can be mined for a variety of health and biomedical research purposes. In Vayena's own words:

> Although these data sets are different from traditional biomedical data, yet the results their analyses yield are of serious biomedical relevance. Analyses of Google searches, Wikipedia searches, social media content, loyalty card points and the like are used to draw a fairly accurate picture of not only our current health but also of our future health, our attitudes towards vaccination, disease outbreaks within our country, and even epidemic trajectories across other continents. In our diverse, evolving data ecosystem it is clear that data generated for a wide range of purposes unrelated to biomedicine still provides rich information about health.[66]

To conclude, we should now take a moment to link what has been said so far about data-driven biomedical research and biomedical big data to the specific focus of this work, in order not to lose its significance in the big picture, which is the conceptualisation of a governance model for biobanks in the digital society. The discussion about data-driven biomedical research and biomedical big data meets our critical reflection on biobank governance in the common ground known as personalised medicine. Indeed, on the one hand, it can be argued that personalised medicine is a big data project, because the main idea behind it is to draw on the various 'omics' data in order to deliver more precise diagnosis and treatment, to predict diseases and eventually to prevent them.[67] On the other hand, biobanks represent one of the key resources and infrastructures for supplying the datasets

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and health care: Ethical issues, 4–18 (Nuffield Council on Bioethics, 2015).

[65] B. D. Mittelstadt & L. Floridi, 'The ethics of big data: current and foreseeable issues in biomedical contexts', (2016) The Ethics of Biomedical Big Data, 445–480.

[66] E. Vayena & U. Gasser, 'Strictly biomedical? Sketching the ethics of the big data ecosystem in biomedicine' in *The ethics of biomedical big data* (pp. 17–39) (Springer, Cham 2016) 23.

[67] Vayena & Gasser (n 52) 'Strictly biomedical?'

that such an ambitious project needs. Therefore, the destinies of personalised medicine and biobanks – both in terms of success and failure – are closely intertwined and depend on how the governance of such a complex research ecosystem – a biobank – is conceptualised. The ethical stakes are very high; such a project: i) impacts on health decisions and patient care; ii) changes the landscape of personal data and privacy; iii) gives patients and participants greater control over their information; iv) poses questions about how to integrate discoveries into medical practices in the context of translational research and also how to combine data from biomedical research (omics) with those from the clinical setting to achieve personalised medicine.[68]

3.2. Research Ethics Committees

Research ethics committees (RECs) are the formal instruments that, in the context of biomedical research, are responsible for reviewing research projects involving humans, from those involving physical interventions to those using stored biological samples and associated personal data. In what follows, for the sake of future analysis, I shall describe their correlation with bioethics, how they are composed, their functions and, finally, the challenges they face with the emergence of data-driven biomedical research.

RECs can be described as a concrete tool for bioethics to ensure the protection of the human rights of the individuals involved in biomedical research and, at the same time, to ensure that scientific interests never prevail over those of individuals. In other words, RECs can be seen as the *trait d'union* between bioethics, human rights and biomedical research, as conceived by Art. 19 of the UNESCO Universal Declaration on Bioethics and Human Rights. The article provides for the establishment, promotion and support at the appropriate level (e.g. regional, national, European and international) of independent, multidisciplinary and pluralist ethics committees in order to:

> (a) Assess the relevant ethical, legal, scientific and social issues related to research projects involving human beings; (b) provide advice on ethical problems in clinical settings; (c) assess scientific and technological developments, formulate recommendations and contribute to the preparation of guidelines on issues within the

[68] F. F. Costa, 'Big data in biomedicine' (2014) Drug Discovery Today *19*(4), 433–440.

> scope of this Declaration; (d) foster debate, education and public awareness of, and engagement in bioethics.

Therefore, firstly, it can be said that RECs are, as argued by de Lecuona:

> The mechanisms that permit […] to step forward from the theory to the action in the different areas where bioethics can operate: assessing methodological, ethical and legal aspects in research; advising on decision-making - often in case of ethical conflicts - in the field of healthcare; advising political powers in the modification or elaboration of regulations and in the design of policies that aim to address with the greatest possible precision the challenges posed by the life sciences, medicine and technologies.[69]

In particular, given the new problems and dilemmas resulting from advances in biotechnology, bioinformatics and genetics and related applications, RECs were initially conceived as forums in which the participation of different disciplines can foster a common reflection in responding to challenges. In turn, the RECs' contribution is to establish the limits of research and medical activity, and what guarantees, and procedures need to be implemented in order to protect the rights of research participants and ensure that scientific and social interests never prevail over the participants' rights and interests.

At a concrete level, ethics committees exist in any public or private research institute or organisation that deals directly with individuals and/or their biological samples and associated data, and they should assess any research projects. Different types of ethics committees exist, with different compositions and different functions, and they are placed at different institutional levels. However, ideally, they must share two common traits: multidisciplinarity and autonomy. Indeed, each ethics committee should be institutionally distinct from the researcher or research sponsor whose project they are assessing, to ensure an independent assessment, reducing the risk of overlooking research issues and decreasing the possibility of conflicts of interest.[70] At the same time, each ethics committee should be composed of experts with different backgrounds in order to bring a range of perspectives to the evaluations. In principle, they aim also to include lay members who

[69] I. de Lecuona Ramírez (n 8) *Los comités de ética,* p.38 (my translation).
[70] A. Ferretti and others 'Ethics review of big data research: What should stay and what should be reformed?' (2021) BMC Medical Ethics, *22*(1), 1–13.

reflect societal interests. Over the 20th century, different types of ethics committees have been established: ethics committees for biomedical research (RECs), clinical ethics committees, national ethics committees and ad hoc committees.

Focusing now on RECs, those related to the issues addressed by this dissertation, their establishment and implementation is regulated at the international level by international governmental organisations such as UNESCO and non-governmental organisations such as the World Medical Association.[71] At the same time, many states have considered it necessary to regulate the conditions of the establishment and functioning of RECs. In this sense, the Spanish case represents a valuable example.[72]

The function of RECs is to evaluate each proposed research project in terms of the design of the study, the scientific validity of the project, the safety and quality of its protocol, the competence and qualifications of the researcher, the procedures that the research project will follow to obtain participant consent and to protect participant data, and the risk-benefit ratio of the project. This is crucial for evaluating whether the rights of the participants or individuals involved will be disproportionately affected.

The arrival of the 21st century, with new challenges in terms of data-driven biomedical research and innovation, has raised fundamental questions concerning the role and scope of RECs as the overseeing body in reviewing the methodological, ethical, legal and societal issues of research projects in scientific research associated with biomedical big data.[73]

Some features, inherent to the way in which biomedical research projects are conducted today, still appear novel to RECs. According to de Lecuona, these features include the fact that 'big data generates an overenthusiasm that impedes the in-depth interdisciplinary reflection necessary to anticipate possible future scenarios, identify conflicts and propose action frameworks and assessment protocols' and the fact that big biomedical research is carried out by multiple bodies, which may have different interests in the data sets.[74]

[71] In particular, the creation and definition of the role of RECs can be traced to the Declaration of Helsinki issued by the World Medical Association in 1964.
[72] Ley 14/2007, 3 July, on biomedical research.
[73] I. de Lecuona, 'Ethics committees: The challenges facing 21st century bioethics' (2011) Asian Bioethics Review 3(2) 164–169.
[74] I. de Lecuona, 'Evaluación de los aspectos metodológicos, éticos, legales y sociales de proyectos de investigación en salud con datos masivos (big data)' (2019) Gaceta Sanitaria, *32*, 576–578.

The way in which data-driven biomedical research challenge ethical oversight mechanisms of biomedical research and biobanks will be critically analysed and discussed in the next chapter.

4. What is a biobank?

A very basic definition of biobank could be 'a large collection of human biological samples and associated data collected, stored and distributed for research purposes',[75,76] but this is not sufficient to convey the reality of a biobank. Indeed, a complete and truthful definition of biobank is that it is a complex system that supports biomedical research by providing high-quality and well-annotated human biological samples. Such activity comprises different dimensions – scientific, technical, economic and ethical-legal-societal – and combines the interests of multiple stakeholders – patients and participants, researchers, biobank staff, patient organizations, public institutions, private partners and general public. The extent of this complex phenomenon and the reasons why biobanks are today the focus of bioethical, legal and political discussion will, I hope, emerge in the course of this dissertation.

Starting with the very basic definition, biobanks collect, store and distribute 'human biological samples'[77] which are constituent parts of the human body or derived from the human body. These may be tissues, blood or blood by products, biofluids (e.g. sputum, urine, bile), cell lines, cell suspensions or isolated DNA or RNA. The origin of these human biological materials differs, they may be obtained from patients with a certain disease in a clinical setting or control groups, voluntary donations, participants of large-scale epidemiological research, or leftover materials after clinical diagnosis or treatment.

Human biological samples are entered into a biobank with their 'associated data' – all relevant personal and health information that may include health records, family history, lifestyle and genetic information but also demographic and lifestyle information, history of illness, treatment and clinical outcomes. It is precisely in this joint and systematic collection

[75] R. Hewitt & P. Watson, 'Defining biobank' (2013) Biopreservation and Biobanking, *11*(5), 309–315.
[76] In this dissertation, I will refer to biobanks only as collections of human biological samples although animal, plant and microbe biobanks are also evolving rapidly alongside human biobanks.
[77] In this dissertation, the terms 'samples', 'biosamples', 'specimens' and 'biospecimens' will be used as synonyms for human biological samples.

of samples and data that the potential of biobanks lies, both to make a difference in biomedical research and, at the same time, to raise ethical and organisational issues.

Depending on how they are categorised once collected and stored in a biobank, biosamples and associated data assume a different 'status' which will also define their ethical and legal destiny. Accordingly, we can distinguish between i) identified samples (i.e. the sample is labelled with direct identifiers, such as name, personal health number, etc.); ii) coded samples (i.e. direct identifiers are removed from the material and replaced with a code); iii) pseudonymised samples (i.e. identifier data are replaced with fake identifiers or pseudonyms); (iv) anonymous samples (i.e. the material never had identifiers attached to it and the risk of the identification of individuals is low or very low).

Moving to clarification of the term 'collection', the collection of human biological samples and associated data for research purposes is a practice with a long history in biomedical research,[78] not a novelty that has appeared since the first appearance of the term 'biobank' in the literature in 1996. However, we can highlight at least four features that help to distinguish biobanks from other medical collections of biospecimens and that apply to any biobank, regardless of its type or use.[79]

First, biobanks collect human biological samples that are annotated with medical and personal data; this coexistence of human biological samples and data is an unavoidable feature of the biobank. Secondly, samples and data are collected in a biobank on a continuous and long-term basis. This leads us to the third feature which is that while biobanks can be associated with current and well-defined research projects, they primarily collect samples and data prospectively for future and unspecified research projects. Finally, biobanks rely on appropriate governance mechanisms and procedures to manage the operation and protect the rights of all the stakeholders involved.

Although this dissertation will approach biobanks as one entity, the existence of many types of biobanks should be noted, with variations depending on the type of research that they intend to support, the types of biological samples that they collect and the collection methods used. Many attempts have been made to classify biobanks and discussion continues.[80] For

[78] They have been called medical repositories, biorepositories and biological resource centres.
[79] L. Annaratone and others, 'Basic principles of biobanking: from biological samples to precision medicine for patients' (2021) Virchows Archiv, *479*(2), 233–246.
[80] P. H. Watson & R. O. Barnes, 'A proposed schema for classifying human research biobanks' (2011) Biopreservation and Biobanking, *9*(4), 327–333; K. Malsagova and others, 'Biobanks—A Platform for Scientific and Biomedical Research' (2020) Diagnostics, *10*(7), 485.

the purposes of this dissertation, a 'first level of categorisation' that acknowledges population-based biobanks and disease-oriented biobanks – as labelled by Annaratone and colleagues – will suffice:

> i) Population-based biobanks provide specimens from individuals of a general population with the aim of studying the role of individual genetic susceptibility and exposure to external factors in the development of specific disorders by linking molecular data with other associated information.
>
> ii) Disease-oriented biobanks collect disease-specific biospecimens. They may be focused on a single type of tissue or include biospecimens from different sources that are relevant to a disease such as cancer.[81]

Finally, it should be acknowledged that biobanks physically comprise a set of freezers and supporting management offices that may be hosted in hospitals, research centres, pharmaceutical and biotechnology companies, patient advocacy organisations or, in some cases, exist as stand-alone organisations.

The culture, values and management of the hosting location profoundly affect the practice of biobanking and establish different priorities. For instance, biobanks located in academic settings or a public-health institution are research-driven, supported by institutional funding and rely on a solidaristic system, whereas industry biobanks are more focused on the final products and are business-oriented.[82]

One word has emerged in the literature that encompasses the reality that I am introducing here: 'biobanking'. Today, the term 'biobanking' covers the collection, identification, storage, control, transportation and disposal of biomaterials and associated data but also, as explained by Malsagova and colleagues, it refers 'to the whole range of social, legal, and ethical problems that must be resolved as biobanks develop'.[83] Indeed, it is important to notice that every phase of biobanking consists of a multilayered and interdisciplinary set of challenges and issues and that the ethical, legal and social issues (ELSI)[84] related to biobanks are considered just as the scientific and technical challenges.

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[81] Annaratone (n 72).
[82] ibid
[83] K. Malsagova and others, 'Biobanks—A Platform for Scientific and Biomedical Research' (2020) Diagnostics, *10*(7), 485.
[84] The acronym ELSI was coined by James Watson, one of the discoverers of the double helix of DNA, who became the director of the Human Genome Institute at the National Institutes of Health in the United States in

Indeed, the two areas are often subject to a process of co-production, as a new scientific issue or technological advance often raises a new ELSI. Furthermore, they have a reciprocal function in solving problems raised in the other area. For example, when it comes to protecting participants' personal data, the question is approached both at a technological level (i.e. double-coding, anonymisation or pseudo-anonymisation of the samples and data) and at an ethical level, establishing whether the participants' personal information is adequately protected and their rights respected.

However, while solutions are usually found for scientific and technological issues through advances in technical tools, informatics and biomedical research, the same cannot be said for ELSI. This is because the latter are the concrete expression of the fact that biobanks are not only scientific infrastructures detached from any context; rather, they elicit questions which by their nature are ethically controversial[85]. In particular, this dissertation will confront with those issues that have ethical, legal and social implications in terms of biobank governance. They are the extent of informed consent, the protection of participants' privacy and confidentiality of personal data, the regulation of secondary uses of collected samples and data. Next to this first level of ELSI in biobanks, a new set of issues has emerged to be addressed in accordance with the evolution of society and new research assets: transparency, participation, public engagement, commercialisation of biobank resources, trust and reputation.

The question of biobank's ELSI will be adequately addressed in the rest of this work. In this paragraph, my aim is to clarify the main concepts characterising biobanks, their function and organization as they will be recurrent topics in this dissertation. Of course, the terminological clarification is merely the prelude to the crucial questions that will be briefly noted here and detailed in the following chapters.

I shall now briefly describe how a biobank works in practice. Rather than going into technical details, I believe that is more important to have an overview of the phases and processes

1988. In the context of the Human Genome Project, the purpose of ELSI research was to predict the potential impact on individuals and society, stimulate public debate, and examine how human genome information can be used to benefit individuals and society, when the human genome is analyzed and sequenced. Today, the acronym ELSI refers to all non-technical issues that arise when developing emerging science and technologies and implementing them in society.

[85] V. Argudo-Portal & M. Domènech, 'The reconfiguration of biobanks in Europe under the BBMRI-ERIC framework: towards global sharing nodes?' (2020) Life Sciences, Society and Policy, *16*(1), 1–15.

that characterise the functions and work of a biobank as a common reference that will allow us to know where to collocate the issues discussed in the following chapters.

Biobanking processes comprise three main phases: collection, storage and distribution.[86,87] The collection phase includes i) informed consent procedures, ii) biospecimen collection, iii) data recording and iv) sample aliquoting preferably with robotic systems.[88] The storage phase regards the act of 'banking' the aliquoted samples at low (-80°) or ultralow (-150°) temperatures in the freezers. In parallel with the physical storage in the freezers, there is a virtual storage process implemented through appropriate management software that, accordingly to Coppola and colleagues, should contain three basic features:

> (i) Biological specimen management (consent management; nonconformity management; and biological resource history related to patients, samples, aliquots, derivatives, storage, and request management); (ii) traceability (follow-up for sample requests, annotation of collections with links to patient files [clinical, genetic, imaging data]); and (iii) interoperability (interface with temperature monitoring systems, interface with the hospital/laboratory to obtain further clinical data).[89]

Finally, the distribution phase involves all the procedures involved in the transfer of annotated samples between biobanks and recipients (internal or external research groups): i) the management and assessment of access requests, ii) the Material and Data Transfer Agreement between the biobank and the researcher, iii) the shipment of samples and associated data to the final recipients.

Moving to the organizational level, one of the key factors that distinguishes a biobank from any other type of research collection, and makes biobanking a valuable area of enquiry from an interdisciplinary perspective, is the fact that it needs an appropriate organisation system

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[86] L. Coppola and others, 'Biobanking in health care: evolution and future directions', (2019) Journal of translational medicine, *17*(1), 1–18.

[87] At a technical level, biobank operations must meet a set of quality and safety control requirements to ensure biological material and data collections of appropriate quality. This is regulated by the International Organization for Standardization (ISO) (https://www.iso.org/home.html) a worldwide federation of national standards bodies that is committed to developing and publishing international standards in the field of technology and manufacturing. In 2018 it issued a document (ISO 20387 https://www.iso.org /obp/ui/#iso:std:iso:20387:dis:ed-1:v1:en) specifically related to biobanking which contains requirements to ensure that biobanks demonstrate competent biobank operations and provide biological material and associated data of appropriate quality for research and development.

[88] The term 'aliquoting' refers to the process of separating portions of biological material in separate tubes.

[89] Coppola and others (n 102) 11.

and governance mechanisms to perform to its full potential as a supporting infrastructure for biomedical research. The importance of a biobank's organisation concerns both the internal setting and the external relationships with other biobanks and research groups.

Many challenges need to be addressed when it comes to designing the internal organisation of a biobank. Annaratone and colleagues summarise this task thus:

> Biobanks represent a fundamental organ to foster scientific research by guaranteeing the quality of results and adherence to standard laboratory practices and ethical requirements. The delicate functioning of biobanks requires governance, organisation (at scientific, technical and administrative levels) and specific funding. Many actors play roles in this process, and the integration of different expertise is key.[90]

Each biobank, depending on its collocation and mission, will usually adopt an organisational structure that is publicly displayed through an organisational chart. This chart should explain immediately how the activities, staff and lines of management of the biobank are organised. Ciaburri and colleagues distinguish between many schemas of recognised organisational structures and conclude that a functional structure that groups all the activities according to a common function seems to best fit the scope, features and mission of biobanks. If the biobank products are high-quality samples and associated data, and the mission of biobanks is to collect, store and deliver them to researchers, the best way to organise this is to foster 'strong inter-relationships between the different activities'.[91]

Following the framework outlined by Ciaburri and colleagues, the application of a functional structure to the biobank's internal organisation should ideally work as follows: biobank activities and staff can be grouped according to their function, namely the operations that they perform. This leads to the individuation of at least three smaller groups based on specialised functional areas: i) the sample and data management group that perform the collection/annotation, storage and shipment, ii) the IT group dedicated to the operation management through the software, and iii) the ethical and legal issues group responsible for informed consent, legal compliance, access governance and material and data transfer agreements. From this first level of organisation, a hierarchical division of roles and

[90] Annaratone and others (no 72) 243.
[91] M. Ciaburri, M. Napolitano & E. Bravo, 'Business planning in biobanking: How to implement a tool for sustainability', (2017) Biopreservation and Biobanking, *15*(1), 46–56.

departments is developed, managed through distinct and clear lines of management, each one reporting to a dedicated person (the biobank director, operational manager, etc.) or oversight body (the scientific committee, ethical committee, etc.).[92]

4.1. Biobank regulation in Europe

Despite the growing importance and key role of biobanks in the context of data-driven biomedical research, the literature on the topic reveals a lack of international common criteria regarding samples and data collection and sharing in terms of quality and safety, and a lack of harmony between legal requirements for biobanking activities across Europe and also at a national level.[93]

To date, the European landscape of biobank regulation is characterised by a mosaic of formal legal instruments[94] as well as informal types of governance tool (e.g. professional guidelines, best practice and ethics documents).[95] The literature on this topic notes the problematic nature of this regulatory diversity because it may hinder the optimal use of biobanks among the scientific community and the release of the full potential for biomedicine advances.[96]

However, it is worth considering that while the need for harmonisation has repeatedly been identified as a condition for European biobanks to be used efficiently, precisely what is

[92] ibid.

[93] K. Beier & C. Lenk, 'Biobanking strategies and regulative approaches in the EU: recent perspectives' (2015) Journal of Biorepository Science for Applied Medicine, *3*(1), 69–81; R. Brownsword, (2011) 'Biobanks, Rights, and the Regulatory Environment' in *Biobanche e informazioni genetiche. Problemi etici e giuridici* (pp. 85-111) Aracne.

[94] Regulations that apply to biobanks: Recommendation CM/Rec(2016)6 of the Committee of Ministers to Member States on research on biological materials of human origin; Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine, Oviedo, Spain,1997; Regulation EU 2016/679 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data.

[95] Soft tools: WMA Declaration of Helsinki on Ethical Principles for Medical Research Involving Human Subjects, Helsinki, Finland, 1964 (last revision 2013); WMA Declaration of Taipei on Ethical Considerations regarding Health Databases and Biobanks, Taipei, Taiwan, 2016; European Commission, *Biobanks for Europe. A Challenge for Governance: Report of the Expert Group on Dealing with Ethical and Regulatory Challenges of International Biobank Research*, Brussels, 2012; OECD - *Guidelines on Human Biobanks and Genetic Research Databases*, 2009; ISBER (International Society for Biological and Environmental Repositories), *Best Practices for repositories: collection, storage, retrieval, and distribution of biological materials for research*, 2012.

[96] S. Slokenberga, O. Tzortzatou & J. Reichel, *GDPR and biobanking: Individual rights, public interest and research regulation across Europe* (Springer Nature 2021) 434.

intended by harmonisation is rarely well defined and seems to express a range of unrealistic expectations. Therefore, a complete unification or standardisation of the ethical and legal frameworks for biobanking is not attainable given the varied nature of biobank initiatives and the different legal frameworks applicable to these initiatives.[97]

Below, I shall briefly describe the ethical-legal framework applied to biobanks in Europe. Starting from the international level, the regulations relevant for biobanks are the European Convention on Human Rights and Biomedicine (the Oviedo Convention)[98], Recommendation CM/Rec 2016(4) of the Committee of Ministers to Member States on research on biological materials of human origin[99] and Regulation EU 2016/679 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data (GDPR)[100].

The Oviedo Convention is a normative document ratified by the majority of Member States that is concerned with preserving rights and fundamental freedoms, such as the integrity, dignity and identity of the human being with regard to applications of biology and medicine, and contains several provisions relevant to biobanks. In particular, two articles merit attention when applied to biobanking: Article 16 stipulates that informed consent is a general rule for research and Article 22 that requires a subject's renewed (secondary) consent if their samples will be used for purposes not covered by the initial consent.[101]

The Recommendation CM/Rec (2016)6 is an updated version of Rec(2006)4 – the first official European statement applying to research with human biological materials – and is intended to cover new developments in the field of biomedical research, in particular in the field of genetics, and increased issues regarding the protection of privacy. Its scope is

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[97] M. Verlinden and others, 'Access to biobanks: harmonization across biobank initiatives' (2014) Biopreservation and Biobanking, *12*(6), 415–422.

[98] Council of Europe, 'European Convention on Human Rights and Biomedicine' April 4, 1997, ETS. no 164, Available at https://www.coe.int/en/web/conventions/full-list?module=treaty-detail&treatynum=164

[99] Recommendation CM/Rec(2016)6 of the Committee of Ministers to member states on research on biological materials of human origins. Available at: https://search.coe.int/cm/Pages/result_details.aspx?ObjectId=090000168064e8ff; Recommendation CM/Rec(2006)4 of the Committee of Ministers to member states on research on biological materials of human origin. Available at: https://search.coe.int/cm/Pages/result_details.aspx?ObjectID=09000016805d84f0

[100] Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (General Data Protection Regulation)

[101] R. Ducato (2010). "Lost in Legislation": il diritto multilivello delle biobanche di ricerca nel sistema delle fonti del diritto (convenzioni internazionali, leggi europee, nazionali e regionali, softlaw) ["Lost in legislation": the Multilevel Governance of Research Biobanks and the Sources of Law (International Conventions, European, National and Regional legislations, Softlaw)].

expanded to cover the collection, storage and use of biological materials of human origin for storage for future research purposes, and those that were previously obtained for another purpose, including a previous research project (secondary uses). It covers cases of secondary use of identifiable biological materials (Article 22), organisational issues (e.g. responsibility for and access to a collection, and quality-assurance measures) (Article 14) and population biobanks (Articles 17–20).[102]

Finally, of significant relevance to the regulation of biobanks in recent years is the adoption of the EU General Data Protection Regulation (GDPR) in 2016 and its applicability from May 2018. It had been long-awaited by the biobank community as a catalyst towards harmonisation in biobank regulation,[103] in particular in relation to the collection, use and processing of personal data – health and genetic data and other information related to individuals – associated with the biobanked samples.

The GDPR sets out binding requirements for the processing of genetic, biometric and health-related data and a set of data subject rights (e.g. the individual's specific consent (Art. 7), right to information, (Art. 12–14), access rights (Art. 15); right to rectification (Art. 16), right to erasure (Art. 17), right to restriction of processing (Art. 18), right to data portability (Art. 20), right to object (Art. 21)), imposing considerable obligations on biobanks and biomedical researchers. Simultaneously it allows for wide-ranging derogations for the purposes of scientific research.[104] Specifically, Article 9(2)(j) permits special categories of personal data (including genetic data and data concerning health) to be processed for scientific research purposes, and in accordance with Article 89(1) genetic and health data processing must be subject to appropriate safeguards for the rights and freedoms of the data subject**.** These safeguards will ensure that technical and organisational measures are in place to respect the GDPR's core principle of data minimisation. However, the GDPR itself provides limited guidance as to the specific safeguards to be adopted since the terms of Article 89(1) are very general. It simply states that personal data should be pseudonymised[105] where possible

[102] K. Beier, & C. Lenk, 'Biobanking strategies and regulative approaches in the EU: recent perspectives' (2015) Journal of Biorepository Science for Applied Medicine, *3*(1), 69–81.
[103] S. Penasa and others, 'The EU General Data Protection Regulation: How will it impact the regulation of research biobanks? Setting the legal frame in the Mediterranean and Eastern European area' (2018) Medical Law International, *18*(4), 241–255; C. H. Ho 'Challenges of the EU 'general data protection regulation' for biobanking and scientific research' (2017) Journal of Law, Information and Science, *25*(1), 84–103.
[104] Slokenberga, Tzortzatou & Reichel (n 79).
[105] Article 4(5) defines pseudonymization as "the processing of personal data in such a way that the data can no longer be attributed to a specific data subject without the use of additional information provided that such information is kept separately and is subject to technical and organizational measure to ensure that the personal data are not attributed to identified or identifiable natural person",

and Recital 33 states that data subjects should be permitted to give their consent in line with ethical standards for scientific research.[106]

When reflecting on the reasons for the lack of harmonisation and shared standards in collecting and processing personal data in biomedical research despite the implementation of the GDPR, it is useful to mention Article 9 (4) of the GDPR which states that 'Member States may maintain or introduce further conditions, including limitations, with regards to processing of genetics data, biometric data or data concerning health'. This tendency to limit EU competence has been described as 'a transition from a "paternalistic" to an "autonomy-based" regime in European data protection'.[107]

In this regard, Marelli and Testa have noticed common constitutive elements between the rise of contemporary biomedicine and the shaping of Europe science policy which, in turn, have informed the structuring of the GDPR:

> (i) a partial retreat of state powers and governing bodies vis-à-vis the advance of market forces and a plurality of heterogeneous "stakeholders," ushering in a substantial reshaping of decision-making ("decentralization"); and (ii) the increased reliance on soft-rule instruments—such as standards, codes of conduct, and ethical thresholds—in place of more rigid forms of legislative interventions ("standardization").[108]

Moving to the specific field of biobanks, one of the most problematic knots of the GDPR concerns exactly how to manage wider consent to the future use of personal data and, consequently, how to accommodate the ethical concerns created by a suspension of individual rights (e.g., the individual's specific consent, right to information, etc.).

In this regards, Recital 33 states:

> It is often not possible to fully identify the purpose of personal data processing for scientific research purposes at the time of data collection. Therefore, data subjects should be allowed to give their consent to certain areas of scientific research when in

[106] C. Staunton and others, 'Appropriate safeguards and Article 89 of the GDPR: considerations for biobank, databank and genetic research' (2022) Frontiers in Genetics, *13*.
[107] L. Marelli & G. Testa, 'Scrutinizing the EU general data protection regulation' (2018) *Science*, *360*(6388), 496–498, 496.

[108] Ivi, p. 496.

keeping with recognised ethical standards for scientific research. Data subjects should have the opportunity to give their consent only to certain areas of research or parts of research projects to the extent allowed by the intended purpose.

However, to date, it is not clear what standard ethical requirements should be adopted in biobanking as additional safeguards alongside the technical and organisational measures mentioned above to mitigate the consequences of the individual loss of autonomy faced by the widening of consent.[109] Therefore, despite the alleged step towards harmonisation that GDPR was expected to bring in the context of research biobanks, many scholars have argued that the only appeal to technical and organisational measures seems inadequate to fulfil the ethical standards of biomedical research.[110]

At the same time, however, the emphasis of the EU legislator on the importance of the ethical dimension, as stated in Recital 33, leaves room for further reflection on the best way to ensure adequate ethical coverage for biobank participants[111] and this is where the ethical framework that I propose in this work aims to find its space.

Before moving to the national level, it is important to mention two instruments of soft law which provide an important ethical reference point at international level for biobanking. I am talking about the Declaration of Helsinki on ethical principles for medical research involving human subjects[112] and the Declaration of Taipei on ethical considerations regarding health databases and biobanks[113].

The first one, whose first version was adopted by the 18th WMA General Assembly in 1964 and amended several times (the last October 2013), is a statement of ethical principles directed at the medical community for medical research involving human subjects and invests biobanks as it includes in its scope also research on identifiable human material and

[109] C. Staunton, S. Slokenberga, & D. Mascalzoni, 'The GDPR and the research exemption: considerations on the necessary safeguards for research biobanks' (2019) European Journal of Human Genetics, *27*(8), 1159–1167.

[110] M. Shabani, G. Chassang & L Marelli. The Impact of the GDPR on the Governance of Biobank Research (2021) In *GDPR and Biobanking* (pp. 45–60). Springer, Cham.

[111] C. Staunton and others, 'Appropriate safeguards and Article 89 of the GDPR: considerations for biobank, databank and genetic research', (2022) Frontiers in Genetics, *13;* D. Mascalzoni and others, 'Are requirements to deposit data in research repositories compatible with the European Union's general data protection regulation?' (2019) Annals of Internal Medicine, *170*(5), 332–334.

[112] World Medical Association. 'World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects' (27 Nov 2013. Available at: https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/

[113] World Medical Association. 'World Medical Association Declaration of Taipei: on ethical considerations regarding health databases and biobanks' (12 Oct 2016). Available at: https://www.wma.net/policies-post/wma-declaration-of-taipei-on-ethical-considerations-regarding-health-databases-and-biobanks/

data. It aims to promote the ethical conduct of research and to protect human subjects from associated risks. The Declaration of Helsinki was the first set of international research guidelines that required research participants to provide informed consent.
The Declaration of Taipei, adopted by the WMA General Assembly in 2016, completes the Declaration of Helsinki providing additional ethical principles for their use in Health Databases and Biobanks indented to cover the collection, storage and use of identifiable data and biological material beyond the individual care of patients.

At the national level, the legislation that applies to biobanks varies from country to country and is in constant evolution, as is the implementation of the GDPR in domestic law. Specifically, we can distinguish between two main situations among the European States:[114] i) countries where specific legislative acts were adopted focusing on biobanks: Spain, Portugal, Belgium, Latvia, Iceland, Estonia, Hungary and Sweden; ii) countries that lack bespoke legislation and rely on composite regulations and soft law tools: Italy, France, Germany and the UK.

Since Italy and Spain are the two countries in which I have conducted my doctoral research, I have had the opportunity to examine and discuss with various experts the national legal frameworks and to appreciate the differences between these two opposing legal approaches to biobank regulation.

Among those countries that have implemented biobank-specific legislation, the Spanish model is one of the most significant. Indeed, Spanish biobanks are regulated by the *Ley 14/2007 de Investigación Biomédica*[115] (LIB) of 2007 which introduced to the European context an innovative framework and legal tool to facilitate the development and regulation of the most cutting-edge fields of biomedical research.[116] In 2012, the LIB was reinforced by the *Real Decreto 1716/2011*[117] concerning the basic requirements for the authorisation and operation of biobanks for biomedical research purposes, the processing of human biological samples and, finally, the creation of a National Registry of Biobanks. We should also

[114] European Commission, Directorate-General for Research and Innovation, 'Biobanks for Europe: a challenge for governance', Publications Office, 2012, https://data.europa.eu/doi/10.2777/68942
[115] Ley 14/2007, de 3 de julio, de Investigación biomédica.
[116] See also C.M. Romeo Casabona, Ley de Investigación Biomédica, Revista de Derecho y Genoma Humano, n.26, 1, (2007); J. Sánchez-Caro & F. Abellan-García Sánchez (2007). Investigación Biomédica en España Aspectos Bioéticos, Jurídicos y Científicos. *Ed. Comares*.
[117] Real Decreto 1716/2011, de 18 de noviembre, por el que se establecen los requisitos básicos de autorización y funcionamiento de los biobancos con fines de investigación biomédica y del tratamiento de las muestras biológicas de origen humano, y se regula el funcionamiento y organización del Registro Nacional de Biobancos para investigación biomédica.

mention the *Ley Orgánica 3/2018*[118] on data protection and the guarantee of digital rights which was enacted in 2018 as a national implementation of GDPR. Although it does not directly refer to biobanks, it regulates the collection, treatment and processing of personal data in biomedical research, which concerns biobank governance.

Title V of the LIB is dedicated to genetic analysis, biological samples and biobanks and is divided into five chapters. Specifically, Chapter IV is focused on the regulation of biobanks and covers many crucial aspects of biobanking, namely the definition and functioning of biobanks, ethical oversight, the ownership of samples, data protection and the matter of informed consent. In particular, it defines and clarifies the legal status of biobanks and differentiates them from other collections of biological samples that could exist for biomedical research purposes. From an organisational point of view, the law states that a biobank must have a scientific director, a data controller and two external committees – one scientific and the other ethical – that will assist the director of the biobank in their functions (Art. 66). The ethical committee, in particular, plays a significant role in biobank governance since it is asked to issue a binding opinion for the authorisation and development of each research project that requests biobanked biological material and data (Art. 60.2). In addition, it exercises the right to authorise exceptions to the general principle of informed consent.

Regarding informed consent, the law states that biological samples collected by biobanks may be used for any biomedical research under the terms provided in this Law, but only when participants have provided their consent (Art. 70.2). Accordingly, the LIB provides for a broad consent; that is, the biobank participant – by a single act of consent at the moment of collection – authorises the use of their samples and data in other future research related to that initially proposed, including research conducted by third parties, without this necessarily being expressed (Art. 60.2).

To sum up, although the Spanish regulations on biobanks have yet to face the novel challenges raised by the new paradigm of data-driven biomedical research, they have the merit of covering many ethical and legal concerns that are strictly correlated with biobanking activities: the legal definition of a biobank, the requirements and management of a biobank, the protection of participants' rights, and informed consent.

[118]Ley Orgánica 3/2018, de 5 de diciembre, de Protección de Datos Personales y garantía de los derechos digitales.

Countries that have not yet adopted biobank-specific legislation could look to the Spanish model as a valuable example, especially for its effort to systematise a field that, at least at the European level, had few precedents in terms of legal frameworks. In particular, the way in which the Spanish regulation approaches broad consent, the role of RECs, the no-commercialisation principle and the focus on the informational nature of human biological samples could provide a useful starting point for those countries now approaching the process of regulating biobanks.[119]

A diametrically opposite situation can be found in Italy which belongs to the group of countries without bespoke regulation for biobanks. To date, indeed, there are no specific provisions applicable to biobanks, and the legal and regulatory frameworks regarding the use of biosamples and related data in research are fragmented[120]. As a result, Italian biobanking activities are currently subject to rules primarily derived from legislation from other biomedical research fields or guidelines and soft law instruments.[121] The first category includes legislation on organ transplantation,[122] blood establishment[123] and medically assisted procreation.[124] A valuable example of a soft legal instrument, conversely, can be found in the *Linee Guida per la creazione, il mantenimento e l'utilizzo di Biobanche Genetiche* developed by the *Società Italiana di Genetica Umana* (SIGU) and *Fondazione Telethon.*[125]

In addition, with the entry in force of the GDPR, the legislation on processing genetic and health-related data relevant to biobanks is articulated in Italy on three levels: the GDPR, the

[119] S. Iacomussi, 'Regulating Biobanks: An ethical analysis of the Spanish law and the new challenges of the big data-driven biomedical research' (2021) RBD. Revista de Bioética y Derecho, 215–233.
[120] To explore the Italian legal framework that regulates biobanking, see M. Macilotti, U. Izzo, G. Pascuzzi G. & M. Barbareschi (2008), La disciplina giuridica delle biobanche, *Pathologica*, *100*(2); C. Casonato, C. Piciocchi & P. Veronesi (a cura di), Forum di Biodiritto 2010, La disciplina delle biobanche a fini terapeutici e di ricerca, Trento 2012.
[121] A. Calzolari, M. Napolitano & E. Bravo, 'Review of the Italian current legislation on research biobanking activities on the eve of the participation of national biobanks' network in the legal consortium BBMRI-ERIC', (2013) Biopreservation and Biobanking, *11*(2), 124–128; R. Ducato, (n 81).
[122] Legge 1.04.1999, n. 91, 'Disposizioni in materia di prelievi e di trapianti di organi e tessuti'.
[123] D.m. n. 78 del 25.01.2001, 'Caratteristiche e modalità per la donazione di sangue e di emocomponenti'.
[124] L. 40/2004, 'Norme in materia di procreazione medicalmente assistita'.
[125] S.I.G.U., Telethon Fondazione onlus, Biobanche genetiche. Linee Guida, pubblicato in Analysis, 5/6 (2003).

Codice in materia di protezione dei dati personali (the Privacy Code)[126] and the General Authorization of the *Garante* for the Personal Data Protection.[127]

To sum up, it can be claimed that there is not a clear regulatory situation, and Italian biobanking initiatives are managed by borrowing rules from other fields. Unsurprisingly, this situation has proved inadequate to cope with the specific issues involved in the storage and use of human biological samples and genetic information – in particular, those concerning the protection of the rights of individuals when it comes to the return of incidental findings, international use, family implications and secondary uses of data.[128]

4.2. The role of biobanks in data-driven biomedical research

It has been repeatedly claimed that biobanks are essential tools in biomedical research. I shall now further explore this assumption. Biobanks are collocated at the point of intersection between several fertile and cutting-edge scientific fields: basic and clinical biomedical research, genetics and genomics, translational biomedical research, big data biomedicine, personalised medicine and epidemiologic studies. Furthermore, biobanking is a field where the potential of innovations in informational technologies, biotechnology and data science converge to produce innovations in biomedical research. For this reason, the more high-quality samples and associated data are available through biobanks, thanks to new knowledge in biotechnology and bioinformatics, the faster biomedical research will advance and impact on the delivery of healthcare to the benefit of society.

This attempt to explore the place occupied by biobanks in the scientific research landscape should be read in the context of a fundamental premise: all the innovations envisaged by translational research and personalised medicine are carried out in a context that has witnessed over the last two decades the transformation of traditional medical research into a data-intensive field. This shift from the analogue to the digital paradigm encourages the cross-border exchange of human biological resources and associated data, and demand is

[126] D.lgs. n. 196/2003 as last amended by D. lgs. n. 101/2018.
[127] Provvedimento Autorità Garante n. 146 of the 5th of June 2019.
[128] C. Piciocchi and others, 'Legal issues in governing genetic biobanks: the Italian framework as a case study for the implications for citizen's health through public-private initiatives', (2018) Journal of Community Genetics, *9*(2), 177–190.

increasing exponentially; hence the central role of biobanks. However, what specifically makes biobanks important for biomedical research today is well explained by Ho:

> Biobanks provide scientific researchers with important resources in two main areas: the interaction between genetic factors underlying common complex diseases and the environment, and the translation of biomedical research into diagnostic and therapeutic applications through pharmacogenomics in pursuit of personalised medicine.

Accordingly, the first area of impact of biobanks is genomics research to support and enhance the potential to identify and understand diseases in terms of their functioning at the level of genes and environmental factors, and their impact on the development of complex diseases. In the field of cancer research, for instance, biobanks currently represent the foundation of three rapidly expanding domains of biomedical science:

> Molecular and genetic epidemiology (aimed at assessing the genetic and environmental basis of cancer causation in the general population as well as in families); molecular pathology (aimed at developing molecular-based classification and diagnostic procedures for cancers); and pharmacogenomics/ pharmacoproteomics (aimed at understanding the correlation between an individual patient's genotype or phenotype and response to drug treatment).[129]

Secondly, we can see the impact of biobanks in translating knowledge from laboratory discoveries to lead to medical applications. Indeed, the second area of biobanks' impact lies precisely in the acceleration and facilitation of this translational process. The technical contribution of biobanks in this process is explained by Mendy and colleagues:

> This is due mainly to technological advances and reductions in the cost of information technology (IT), used for data storage and for the assembly, evaluation, and analysis of large numbers of samples, as well as increases in analytic capabilities and the drastically reduced costs of DNA sequencing, with results available within a shorter time frame. Similar advances in mass spectrometry have drastically lowered the cost

[129] M. Mendy and others, *Common minimum technical standards and protocols for biobanks dedicated to cancer research* (IARC Techn. International Agency for Research on Cancer, Lyon 2017)

> and expanded the ability to characterize proteins and the metabolites present in biological samples.[130]

Beyond the technical aspects, the impact of biobanking on the development of personalised and precision medicine is potentially crucial.[131,132] Personalised and precision medicine, indeed, is the goal of the digital revolution in biomedical research, seen as:

> A medical model using characterisation of individuals' phenotypes and genotypes (e.g. molecular profiling, medical imaging, lifestyle data) for tailoring the right therapeutic strategy for the right person at the right time, and/or to determine the predisposition to disease and/or to deliver timely and targeted prevention.[133]

Accordingly, biobanks are seen potentially as the best supporting tool in the identification of new biomarkers and in the elucidation of the etymology and molecular basis of complex diseases.[134]

To sum up, the key message here is the recognition of the concrete contribution made by biobanks in a period of great fertility of biomedical research driven by large-scale data collection. Biobanks are today the meeting point of different, highly advanced scientific fields that all rely on them to produce advances and innovations. Biobanks guarantee a systematic and high-quality collection of well-annotated human biological materials and well-organised and up-to-date databases. In a nutshell, we can say that how biobanks are designed, structured and governed determines the success or failure of such innovations.

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[130] Ivi, p. 5.
[131] R. E. Hewitt, 'Biobanking: the foundation of personalized medicine', (2011) Current Opinion in Oncology, *23*(1), 112–119; A. Liu & K. Pollard, 'Biobanking for personalized medicine', (2015) Biobanking in the 21st Century, 55–68.
[132] For a critical analysis of the scope and potential of personalised and precision medicine see: G. Boniolo, 'The problematic side of precision medicine' 2022. In *Can Precision Medicine Be Personal; Can Personalized Medicine Be Precise?* Oxford University Press.
[133] Council of Europe, Conclusions on personalised medicine for patients https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=OJ%3AC%3A2015%3A421%3AFUL Accessed 3 Feb 2022.
[134] J. Kinkorová, 'Biobanks in the era of personalized medicine: objectives, challenges, and innovation', (2016) EPMA Journal, *7*(1), 1–12.

5. What is governance?

In recent decades, the concept of governance that originated in political theory and discussion, as opposed to a centralised and sovereign state, has spread to other disciplines producing, thus, an intensive use, and sometimes misuse, of the term. Since I have decided to use this word in the title of the present work and to make the concept of governance one of the main pillars of my dissertation, in what follows I shall try to clarify how I intend to use this concept in relation to biobanks. After a brief overview of the definition of governance and its origins, I will frame the question of what precisely governance refers to in the context of biomedical research and how the concept of biobank governance will be approached in the next chapters.

The definition of governance varies depending on the field concerned, but a common thread – informative about how the concept is used – can be found in its history. Before it became pervasive, the concept of governance emerged in the early twentieth century – as described by the philosopher Bevir – when new social theories and practices began to '[draw] the attention away from the central institutions of the state and towards the activity of governing, and much of the activity of governing involves private and voluntary organisations as well as public ones'.[135]

Accordingly, developed in contrast with the notion of a government focused on the state and institutions, governance refers to the process of governing and its expression in social practices and activities.

Following Bevir's argument, some features of governance derive from its original field of enquiry. First, the fact that at a political level governance arrangements are often hybrid practices, combining established administrative arrangements with private-sector influences in the form of market strategies and mechanisms. Secondly, governance and its mechanisms are usually multi-jurisdictional and translational: indeed, 'current patterns of governance combine people and institutions across different policy sectors and different levels of government (local, regional, national, and international'.[136] Finally, governance

[135] M. Bevir, *Governance: A very short introduction* (Oxford University Press, 2012) 1.
[136] Ivi, p. 6

moves away from formal institutions, recognising more diverse informal practices as well as an increasing range and plurality of stakeholders. Since the 1990s, the term governance, and its implementation in different sectors, has taken on many different meanings. Rhodes, one of the main scholars of the notion, has identified six different applications of the idea: the notion of the minimal State, corporate governance, new public management, good governance, socio-cybernetic systems and self-organising networks.[137]

Outside the political sphere, the concept of governance today, in contrast to top-down mechanisms of power and rigid procedures, evokes a plurality of values and visions. In particular, regardless of its field of application, reference to governance should draw attention to the possibility that rules and control can emerge from the actions of all the actors involved and, thus, to opportunities to rethink the criteria of entitlement to decision-making power.

Taking all these inputs together, for the purposes of this dissertation, the notion of governance can be understood as a combination of hybrid mechanisms put in place to govern something. These mechanisms are created by rules, processes and behaviours that arise from contributions from different fields (e.g. ethics, regulation, market strategies) and people.

In order to enrich this understanding of governance, we can juxtapose the concept of governance with two other concepts – regulation and organisation – that are closely related to it and with which it may be confused. When founding and deciding how to organise a public or private activity, institution, infrastructure or company, the term 'regulation' refers to formal structures of law and legally constituted regulatory bodies, whereas 'governance' is an overarching concept that includes regulation but also all the other less formal documents and procedures that can dictate behavioural norms in a specific context. In the same way, governance is broader than the term 'organisation' or 'structure', as its sense is more abstract. Indeed, as governance regards the process of governing, it cannot be reduced to a description of activities and rules, given that it concerns also the approach and the philosophy behind them.

The notion of governance is frequently coupled with the adjective 'good', and references to 'good governance' (meaning 'governing well') have become a mantra for public and private

[137] R.A.W. Rhodes, *Understanding Governance. Policy Networks, Governance, Reflexivity and Accountability* (Open University Press 1997).

organisations, companies and institutes. What constitutes good governance? The success of a governance framework is usually measured based on its adherence to certain principles.

In its white paper on governance,[138] for instance, the European Union counts among the principles of good governance openness, participation, accountability, effectiveness and coherence. In this specific context, the adherence to and application of these principles permit the EU mission to flourish in implementing new policies and actions. The same applies to any other institution that wants to enhance its integrity and efficiency: it must outline its principles of good governance, and design and implement procedures in accordance with them.

Based on the above considerations, I shall now explore the application of the concept of governance to the field of biomedical research in an attempt to come closer to a clarification of what biobank governance means and how the topic will be approached in the remainder of this work.

In the introduction to *Ethics and Governance of Biomedical Research: Theory and Practice*, Strech and Mertz define governance in biomedical research as follows*:*

> Governance of biomedical research can be understood as an umbrella term that covers the following: (a) the rather narrow field of research regulations in the sense of laws and legal authorities or oversight bodies; and (b) the broader field of guidelines, […] advisory boards, editorial policies, ethics codes, and public involvement activities and other efforts that exist to promote the ethical conduct, social value, and appropriate freedom of biomedical research.[139]

We can recognise in this definition some of the features of the concept of governance that we have observed above. Therefore, talking about governance in biomedical research means recognising and acknowledging the coexistence of different levels of power from the most institutional level – represented by the law and formal authorities – to that drives more informal and internal mechanisms and relationships. Further, the definition acknowledges

[138] 2001 EC White Paper on European Governance.
[139] D. Strech & M. Mertz (Eds.) *Ethics and Governance of Biomedical Research: Theory and Practice* (Vol. 4) (Springer 2016) 2.

the interaction between different levels of activity conducted by different stakeholders, from members of the advisory boards to the general public.

Furthermore, as in other fields, the field of biomedical research is not immune to demands for good governance. The primary core values and normative principles on which governance mechanisms are based in biomedical research are summed up by Strech and Mertz as follows:

> Safeguarding social value and scientific validity of research (making research worthwhile); enabling a favourable risk-benefit ratio for research participants (countering excessive maleficence); allowing for independent review of study protocols (e.g., preventing questionable conflicts of interest); ensuring informed consent and a fair selection of participants (avoiding discrimination and exploitation); maintaining respect for participants during research (promoting health and their sense of self-worth); and establishing collaborative partnerships, including the fair and transparent dissemination of the research results.[140]

To conclude this very brief explanation of the application of the concept of governance to biomedical research, it is worth mentioning a more abstract account, supported by Bonino and colleagues, that speaks for an inclusive and participatory approach to research and healthcare and should, I believe, be welcomed in a heuristic sense. The authors argue that the concept of governance in biomedical research should be understood as an open, ethical, political and legal 'scenario' for the achievement of a progressive and constantly progressing collaboration between all the parties involved in defining the path and the rules of the direction of the research. In the words of the authors:

> The relevance of governance as a political and legal scenario lies in the opportunity to look at relations in the sphere of health in a different way; in the possibility of linking through an open dialogue the dichotomies between expert and non-expert knowledge, between technoscience and ethics, between public powers and individual autonomy.[141]

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[140] Ivi, p. 2.

[141] A. D. F. Bonino and others, 'Governance e salute: un laboratorio tra ricerca e cura', *Notizie di Politeia* (2006) [Original quotation: "La rilevanza della governance come scenario politico-giuridico consiste nella opportunità di guardare alle relazioni nella sfera della salute in modo diverso; nella possibilità di ricollegare in relazione discorsiva le dicotomie tra saperi esperti e non, tra tecnoscienza ed etica, tra poteri pubblici e autonomie individuali."]

5.1. Biobank governance

The concept of governance is easily applicable to the field of biobanking since, as we have delineated in this chapter, a biobank is a complex organisation that involves multiple stakeholders, operates at the intersection of different formal and informal regulatory frameworks, relies on multi-jurisdictional and transversal networks and international sharing and depends on a careful combination of mechanisms, processes and practices.

In the following, I will attempt to clarify how – through which mechanisms – governance is enacted in biobanks.[142] I will then conclude by explaining my approach to biobank governance and presenting an understanding of the concept that will guide us throughout the dissertation.

On the very first level of reading, we can refer to biobank governance every time it comes to define and explain how a biobank is internally organised, how the functions are distributed, how the decision-making processes are allocated and who is accountable for what. Accordingly, each biobank usually develops and publicly displayed a model or framework of governance that shows the internal organisational structure of the biobank with the list of biobank's personnel, the daily management of activities, the function and composition of the committees (i.e., scientific, ethics, access, advisory) and an oversight of its general mission and strategic policy. In other words, a biobank governance model usually defines all the people, policies and procedures that are required to enable the correct functioning of the biobank.

A second broader level of reading is the one that emerges from the definition of the European Commission's expert group on biobanks who have claimed that in the field of biobanking,

> Governance can consist of formally-constituted regulatory bodies, statute and other legal instruments, as well as informal mechanisms such as advisory boards, professional guidance, biobank policies and professional values and culture that help to guide decision-making. The component elements of governance are therefore

[142] E. Rial-Sebbag & A. Cambon-Thomsen, 'The Emergence of Biobanks in the Legal Landscape: Towards a New Model of Governance' (2012) J. of Law and Soc. 39(1) 113–130; J. Kaye and others, *Governing Biobanks – Understanding the Interplay between Law and Practice* (Hart 2012); J. Kaye, 'From single biobanks to international networks: developing e-governance', (2011) Hum. Genet. 130(3) 377–382.

> people (individual decision-makers as well as institutions), procedures, policies and everyday practice.[143]

Therefore the mechanisms that carry out governance in biobanks are varied and of different nature: they can consist of documents such as national and international legislations, regulations, ethical guidelines, codes of conduct and policies about samples and data access; procedures such as safety and quality control, decision-making process of ethical committees and other oversight bodies are put in place to support those documents and they can be informal and implicit actions reflecting 'how things must be done' as well as formal procedures in compliance with the law and current regulations[144]. All these elements put together constitute the process of governing a biobank that can be defined as 'all formal and informal policies, processes, and structures that guide the activity of a biobank'[145].
As pointed out by Kaye, the benefit to have an adequate governance model for biobanks is that:

> It promotes certainty and efficiency as people know what the rules are, what happens, and when. It can ensure uniformity and equality—that things are done in a uniform way with everyone and the same issues being treated the same. Such a system enables problems to be anticipated as there are mechanisms to deal with the routine issues but unanticipated situations can also be resolved efficiently. Having a governance system in place ensures that ethical and lawful research is supported through accountable and transparent decision making.[146]

Furthermore, as in other areas, we also talk about good governance in biobanking, and values and principles need to be set in accordance with the mission of the biobank, the interests of all the stakeholders and the expectations of the public. The International Agency for Research on Cancer (IARC), for instance, has claimed that good governance for cancer-oriented biobanks should:

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[143] European Commission, Directorate-General for Research and Innovation, *Biobanks for Europe: a challenge for governance* (Publications Office, 2012) https://data.europa.eu/doi/10.2777/68942
[144] J. Kaye, 'From single biobanks' (n 140).
[145] F. Gille, E. Vayena & A. Blasimme, 'Future-proofing biobanks' governance' (2020) European Journal of Human Genetics, *28*(8), 989–996.
[146] J. Kaye, 'From single biobanks' (n 140).

> Ensure that the biobank remains faithful to its purpose, encouraging trust between the various stakeholders; be guided by a set of overarching principles when making decisions, including being transparent, accountable, consistent, proportionate, efficient, coordinated, equitable, and fair; and be dynamic and able to adapt over time.[147]

When we combine these different readings of biobank governance, it can be said that the concept of biobank governance that permeates this thesis incorporates various insights. First, biobank governance will be regarded as an ongoing process formed by actions, decisions and practices guided by ethical principles in line with multiple stakeholder expectations and interests, through which the biobank develops and is sustained. Secondly, this dissertation will consider a further, most abstract, level of understanding of biobank governance, which focuses on biobanks not simply as an object or topic of governance but also how they can be seen as an entity through which the governance of life operates. The potential of such a change of perspective, one that transforms biobanks from objects of a study on governance mechanisms to subjects that can govern in their own right has been stressed by Gottweis and Peterson, who coined the expression 'governing through biobanks'. In their own words:

> Biobanks are not only 'topics' and 'problems' of governance, they articulate particular rationalities and constitute a complex process of representing science, bodies, medicine and technology. They are a form of governing life and involve a multitude of actors such as scientists, patients, or industry who actively engage in building, describing and operating biobanks and who contribute to translating particular scientific-technological visions into material practices.[148]

[147] Mendy and others (n 128).
[148] H. Gottweis & A. Petersen (Eds.) *Biobanks: governance in comparative perspective* (Routledge 2008) 9.

5.2. Governance broader than ethics

In clarifying and proposing a governance model for biobanks in the digital society, a key point of reference will be the Responsible Research and Innovation's paradigm (RRI)[149] adopted by the European Commission since 2013 at the launch of the Horizon 2020[150] project as a strategic approach to governing research and innovation through the lens of responsibility. In particular, RRI is committed to maximising the value of publicly funded research so that it may in return benefit society. It encourages the production of innovations through social engagement and collaborative research, and requires close cooperation between all stakeholders involved in the research and innovation process, both from the public and the private sectors.[151]

The RRI framework comprises a policy agenda of five actions (governance, ethics, public engagement, science education, open access and gender equity) that should be implemented as a package in the context of those projects, activities, organisations, institutions, companies and industries whose main assets are scientific research and innovation.[152]

The main objective of RRI is to create high-quality science aligned with the values, needs and expectations of society. Accordingly, two principal outcomes are expected from the implementation of RRI in all the phases of the research process and its translation to innovations. First, implementing RRI is expected to lead to a more engaged public, responsible actors and responsible institutions. Secondly, the implementation of RRI aims to make science and technology more ethical, sustainable and socially beneficial by including more voices in research and development and making adaptive changes to

[149] R. Owen and others, 'Responsible Research and Innovation: From science in society to science for society, with society' (2012), Science and Public Policy (39) 751–760.

[150] The EU's research and innovation funding programme from 2014 to 2020 with a budget of nearly €80 billion. Available at https://ec.europa.eu/info/research-and-innovation/funding/funding-opportunities/funding-programmes-and-open-calls/horizon-2020_en. Accessed 10 March 2022.

[151] Communication from the Commission, Europe, *A Strategy for Smart, Sustainable and Inclusive Growth* (COM (2010) 2020 final); European Commission, Horizon 2020 EU Framework Programme for Research and Innovation—Responsible Research and Innovation, https://ec.europa.eu/programmes/horizon2020/en/h2020-section/responsible-research-innovation Accessed 14 Feb 2022.

[152] I. de Lecuona & G. Rabal, 'MICROBiome-based biomarkers to PREDICT decompensation of liver cirrhosis and treatment response' (2019), Deliverable 8.1 MICROB-PREDICT Project. Available at: https://microb-predict.eu/ Accessed 1 March 2022

achieve this. In doing so, RRI generates outcomes that are ethically acceptable, sustainable and more useful to society in the long term.[153]

To achieve these outcomes, RRI contains four dimensions of the research process that attempt to reflect the social, ethical and political stakes associated with technological and scientific advances: diversity and inclusion, openness and transparency, anticipation and reflection, responsiveness and adaptation. Thus, the research and innovation process should be diverse and inclusive to produce outcomes aligned with the values and expectations of society since they take into account different perspectives and expertise; open and transparent to make the process of research and innovation more accessible to all actors, allowing people to discuss and scrutinise science and technology and thus empowering them to make more informed decisions; anticipative and reflective to envision impacts and reflect on the underlying assumptions, values and purposes of the research, allowing more responsible action; and responsive and adaptive to change to respond to views expressed by stakeholders, changing circumstances or new knowledge.[154]

At a closer look, these dimensions can be considered to equate with good governance principles. Unsurprising, indeed, they reflect the five requirements that in the EU context underpin good governance: openness, participation, accountability, effectiveness and coherence.[155]

At this point, it is worth taking a moment to reflect on the degree to which the discussion so far on biobank governance can be read in parallel with an RRI framework. As largely argued in the previous paragraphs, biobanks are today a key element in the production of research and innovation in the biomedicine sector. For this reason, a discussion on the best model of biobank governance in the digital society in Europe cannot be separated from a discourse on RRI and its challenging application in the field of biobanking.[156]

For the purposes of this work – and in particular for my proposal of a governance model for biobanks in data-driven biomedical research – I am interested in how the concepts of governance, ethics and public engagement are developed within the framework of RRI and, in turn, how my proposal can be aligned with them. Governance is described as an umbrella

[153] Shaping the future: A Responsible Research and Innovation policy brief https://rri-tools.eu/
[154] ibid.
[155] 2001 EC White Paper on European Governance.
[156] H. Yu, 'Redefining responsible research and innovation for the advancement of biobanking and biomedical research' (2016) Journal of Law and the Biosciences, *3*(3), 611–635.

term for activities that aim to address questions related to the processes and procedures that can be implemented to ensure responsible research and innovation. In turn, it represents a key policy agenda because it provides a structure that includes policies, rules and processes and affects how powers are exercised in the process of translating discoveries to innovations.

Ethics is considered an integral part of research throughout the entire process, and ethical compliance is seen as pivotal in achieving real research excellence, as such research needs to be morally grounded and acceptable to society. The core ethical principles for research and innovation are those relevant at the levels of national, EU and international legislation, including the UNESCO Charter of Fundamental Rights[157] and the Council of Europe's Oviedo Convention.[158] Particular attention is given to the principle of proportionality, the right to privacy, the right to the protection of personal data, the right to the physical and mental integrity of a person, the right to non-discrimination and the need to ensure high levels of human health protection.[159]

Alongside governance and ethics, public engagement is considered one of the key points in RRI, which is committed to the possibility of co-creating the future of research and innovation with citizens and civil society organisations. Indeed, public engagement is understood as a way to include the widest possible diversity of actors, those who would not normally interact with each other on matters of scientific and technological research and progress. It involves embracing the idea of a publicly engaged science in which public engagement is implemented through open and inclusive strategies that allow input from the relevant participants. In line with the participatory turn occurring in the field of health research and care, expert opinions will still be crucial in decision-making, but the input of research participants and citizens will become increasingly relevant.[160] At the same time, public engagement within the RRI agenda is understood as a way to overcome traditionally one-way scientific communication and contribute to making science more open and transparent.

[157] UNESCO 'Universal Declaration on Bioethics and Human Rights', 19 October 2005. Available at: https://unesdoc.unesco.org/ark:/48223/pf0000146180 Accessed 20 March 2022.
[158] Council of Europe, 'European Convention on Human Rights and Biomedicine' April 4, 1997, ETS. no 164, Available at https://www.coe.int/en/web/conventions/full-list?module=treaty-detail&treatynum=164
[159] Regulation (EU) No 1291/2013 of the European Parliament and of the Council of 11 December 2013 establishing Horizon 2020 - the Framework Programme for Research and Innovation (2014–2020) and repealing Decision No 1982/2006/EC Text with EEA relevance.
[160] L.E. Siffels & others 'The participatory turn in health and medicine: The rise of the civic and the need to 'give back'in data-intensive medical research' 2021 Humanities and Social Sciences Communications 8(1) 1-10.

Therefore, setting up a participatory research agenda is considered a top priority under this framework, and this has multiple advantages. First, it helps to identify stakeholders' unmet needs and what matters to them. Secondly, it encourages researchers to include new perspectives in research and, at the same time, it prepares 'lay' stakeholders for the research process. Finally, it enables and empowers stakeholders to develop their own voice.[161]

To conclude, my proposal for biobank governance embraces the concepts of governance, ethics and public engagement proposed by the RRI framework. In particular, I am interested in exploring a conceptualisation of biobank governance – understood as a structure informed by the right principles that provide the right conditions of existence – with two complementary aspects: a set of ethical procedures, practices and policies aligned with biobank stakeholders' interests, and a set of public engagement strategies that provides the basis for such ethical procedures, being committed to listen to and include all voices, values and expectations.

With this concept of governance in mind, I believe that in what follows it will be possible to make progress in two complementary directions: at a macro level, the much-needed effort to reassess bioethical guidance in a way that is better suited to cope with the challenges of the digital society and, for my specific goal, to address the ethical, legal and social issues related to biobanks.

Accordingly, this understanding of governance better fits as an additional but complementary element of the existing ELSI framework for biobanks and aligns with a growing trend in the literature on certain tangential topics (e.g. the ethics of Artificial Intelligence, digital ethics) that use the acronym GELSI to refer to Governance, Ethics, Legal and Societal Implications as a whole.[162] I believe that, read together with ELSI, the sense of studying biobank governance reaches its fullness of meaning. That is, governance is both the scenario and the field of action against which ELSI can be embraced, understood and concretely solved and improved.

Moreover, I believe that assessing and conceptualising the role of biobanks in a digital

[161] https://rri-tools.eu/public-engagement

[162] J. Desai and others, 'The epistemological foundations of data science: a critical analysis' (2022) SSRN Electronic Journal. Available at SSRN: https://ssrn.com/abstract=4008316 or http://dx.doi.org/10.2139/ssrn.4008316 Accessed 14 Feb 2022; M. Taddeo, 'The ethical governance of the digital during and after the COVID-19 pandemic' (2020) Minds and Machines, *30*(2), 171–176.

society under the overarching aspect of governance is an opportunity to elevate the discussion beyond legal compliance with regulations and to engage with a moral evaluation of procedures, a better clarification of the concepts involved and an identification of unsolved problems and new challenges.[163] Therefore, this thesis will approach the study of biobank governance as 'an opportunity to innovate regarding modes of governance beyond formal, public, or positive law; beyond publicly enacted regulation'.[164]

This intention aligns with the challenge posed recently by the philosopher Floridi regarding the governance of the digital. Considering that the biobank field in Europe is characterised in most countries by regulatory uncertainty, a lack of legal harmonisation at the international level and confusion regarding appropriate safeguards under the research-related derogations of GDPR, the pursuit of ethical standards should be sought elsewhere. Therefore, I believe that the focus should be on identifying – in the context of biobanking – those ethical principles that can adequately inform biobank governance in order to complement the legal gap. Following Floridi's approach, biobank governance represents a compelling case in which it is necessary to engage in ethical evaluations 'over and above the existing regulation, not against it'. The challenge is to rethink biobank governance and its guiding principles in such a way that it can promote the highest ethical standards in practices, procedures and policies – especially regarding participant protection and the RRI agenda – as a way to bridge the gap between legal and ethical domains.

[163] L. Floridi, 'Soft ethics and the governance of the digital' (2018) Philosophy & Technology, *31*(1), 1–8.
[164] M. Madison, in T. Minssen, J. R. Herrmann & J. Schovsbo (Eds.) *Global Genes, Local Concerns: Legal, Ethical, and Scientific Challenges in International Biobanking* (Edward Elgar Publishing 2019) 27.

6. Conclusions

In this chapter, I have addressed the existing questions that I believe to be crucial to this dissertation, given its goal of conceptualising a governance model for biobanks in a data-driven biomedical research context. The topics that I have covered are bioethics, biomedical research, biobanks and governance, since they are essential to the development of the present work. Starting from four general questions (What is bioethics? What is biomedical research? What is a biobank? What is governance?), I have developed sub-questions and answers that have allowed me to cover all the main concepts involved in the dissertation. The aim was to provide a common set of definitions and connections to clarify to the reader the context of my research. I now recall the key points to be taken into account in the continuation of this paper.

First, this dissertation is permeated by an understanding of bioethics as conceptual analysis and the clarification of issues, arguments and principles related to the ethical challenges raised by biotechnology and our digital society to biomedical research, and their implications for biobank governance, driven by philosophical reasoning and bound with human rights. Therefore, in the next chapters, I will conduct a bioethical enquiry, driven by a philosophical questioning spirit and a normative power that allows this research to be incisive on the novel challenges faced as well as to move away from some of the ethical dogma that has brought research ethics to a standstill. Accordingly, this work will closely follow the evolution of bioethics in the digital society, using biobanks as a point of observation and a testing ground for the conceptualisation of a more appropriate ethical framework for biomedical research and biobanks.

Secondly, I have applied the same approach looking forward to the future in addressing the question of what biomedical research is. After giving a general definition of basic, clinical and translational research and the role of RECs in assessing biomedical research projects, I have shifted focus to the direction of future biomedical research, concluding that this is primarily data-driven. Accordingly, particular attention has been paid to clarifying how biomedical research is conducted today and to a description of the phenomenon of biomedical big data, preparing the ground for the description of the role of biobanks in this new research asset.

Indeed, I have defined biobanks as key infrastructures for fostering research and innovation in the context of data-driven biomedical research. They achieve this by ensuring a

systematic and high-quality collection of well-annotated human biological materials and well-organised and up-to-date databases.

It goes without saying that such expectations and pressure on biobanks in their supporting role in fostering goals of translational research and personalised medicine should prevent any further postponement of a conceptualisation of biobank governance in the digital society, especially in the light of the extremely fragmented biobank regulation across Europe, the number of ELSI brought by the new research asset and the presence of multiple stakeholders whose voices must be heard to ensure the viability of biobank projects.

Following this reasoning, I have, lastly, addressed the question of what governance is, by specifying what is meant by biomedical research governance, and by reflecting on the best possible understanding of governance to be applied to biobank in the current research asset.

I have suggested, in conclusion, that ELSI in biobanks should be considered in the scope of the concept of governance presented in the RRI framework provided by the European Commission, as part of a politics focused on the alignment of societal interests with the progress of science and technology.

Therefore, my proposal will rely on an account of governance inspired by that promoted by the RRI framework that, in my opinion, has the merit of conveying an understanding of governance which is broader than ethics and is committed to providing a suitable structure – comprising policies, rules and processes inspired by its principles – to implement ethical procedures that align biobank research with participants and society' interests

Chapter 2
Detecting the ethical challenges for biobanks in data-driven biomedical research

1. Introduction

This dissertation designs data-driven biomedical research as the background against which conceptualise a model of biobank governance. In this chapter, I conduct a critical analysis to understand the features of data-driven biomedical research that may currently affect, influence or present challenges to biobanks in order to lay the foundations for the conceptualisation of an appropriate model of governance in the next chapter.

I identify two main contextual problems that have had a significant impact on biobank governance. Firstly, the digital paradigm in biomedical research implies new challenges for traditional concepts of research ethics, in particular privacy, informed consent and ethical oversight mechanisms, and renders the existing ethical framework inadequate to protect research participants and, in our case, biobank participants. Secondly, data-driven biomedical research responds to a precise political, economic and societal 'plan': the commitment of the European Union to a data-driven economy. This context increases the risk of price prevailing over the value of research and, accordingly, the trend towards the commodification of the human body, its parts and associated data corrupts other values inherent to research, such as common good, benefit-sharing, solidarity and justice.

On the basis of this premise, the first part of the chapter addresses the implications that the transition from analogue to digital society has brought to the field of biomedical research in terms of epistemological, practical and ethical challenges. Specifically, I analyse the emergence of the digital paradigm in biomedical research against traditional framework to show that existing ethical frameworks are no longer sufficient to ensure the protection of research participants and I discuss the ELSI of biobanks with a focus on the core of the ethics of biobanking and on emerging trends.

The second part of the chapter addresses the question of how the market and the data-driven society influence biomedical research. After a brief description of the political, economic and social commitment of the European Union towards a data-driven economy and society, I analyse the trends towards the commodification of human biospecimens and

associated data against the principle of non-commercialisation of the human body that informs the research ethics framework. Accordingly, two cases are presented to support the argument that this trend is already widespread and to help clarify the relevance of the ethical issues at stake.

The final part of the chapter analyses in detail the implications of the context described for biobank governance. First, it discusses the issue of private intermediaries seeking access to biobank samples and data to trade them in exchange for money without the knowledge of the biobank participants. Secondly, I argue that the conceptualisation of biobank governance in data-driven biomedical research needs start from an acknowledgement of what is wrong with the commodification of biobank samples and data and, equally, an acknowledgement that greater effort should be put into accommodating the data-centric nature of biobanks from both a regulatory and an ethical perspective.

2. The emergence of the digital paradigm in biomedical research

The focus of this section is a critical analysis of the conditions and implications of the transition to a digital society in biomedical research and, in turn, for biobank governance in order to demonstrate that the traditional research ethics framework now fails to provide adequate guidance.

Firstly, I identify the transition from analogue to digital society as the main trigger of the ethical challenges facing biomedical research and, specifically, biobank governance as addressed by this dissertation. This transition is defined by all the societal, technological, economic and political processes that have in recent decades led to the adoption and integration of ICT in every single sphere of our lives at work and home, in education, health and recreation. The result of this process is an ICT-dependent society, in which the creation, distribution, use, integration and manipulation of information and data have become the main economic, political and cultural activities.[165]

[165] I. V. Lokshina, B. J Durkin & C. J. Lanting, 'Internet of Things and Big Data-Driven Data Analysis Services for Third Parties: Business Models, New Ventures, and Potential Horizons' in N. Meghanathan (Ed.), *Strategic Innovations and Interdisciplinary Perspectives in Telecommunications and Networking* (pp. 256–289) (IGI Global 2019). https://doi.org/10.4018/978-1-5225-8188-8.ch014

A society defined in this way reaches a point where, according to Floridi's analysis of the 'infosphere', 'ICTs and their data processing capabilities are not just important but essential conditions for the maintenance and any further development of societal welfare, personal well-being, and overall flourishing'.[166]

Concrete examples of so-called digital societies include the member States of G7, i.e. Canada, France, Germany, Italy, Japan, the UK and the USA, as in each of these countries 'at least 70 per cent of the Gross Domestic Product […] depends on intangible goods, which are information-related, rather than on material goods, which are the physical output of agricultural or manufacturing processes'.[167]

The transition from analogue to digital society, which has triggered the main transformative developments in the context of my research, is described by Floridi as that span in which society has completed the transition from history to hyper-history, in which ICT has 'evolved from being mainly recording systems, to being communication systems, to being also processing systems which basically means that thanks to this evolution nowadays we depend on information-based and intensive services and information-oriented public sectors'.[168]

My understanding of the digital society is based on these definitions. I rely on Floridi's critical analysis because I share his view that it is necessary to draw a new conceptual framework to give significance and meaning to new phenomena and understand the complexity of our current situation.[169] In particular, what Floridi proposes to do at the philosophical level – finding new philosophical categories to understand the transformations brought by the digital society to our conception of history, the environment and ourselves – must, I believe, also be done at the bioethical level. Finding the most appropriate ethical guidance for our digital society is essential in integrating the existing framework of research ethics that – as we will see below – has proven to be insufficient and, in turn, providing the optimal conditions to empower citizens through ethical practices in a changing world without definitive reference

[166] L. Floridi, The Fourth Revolution: How the Infosphere is Reshaping Human Reality (Oxford University Press 2014) 4.
[167] ibid.
[168] L. Floridi, 'The information society and its philosophy: Introduction to the special issue on 'the Philosophy of Information, its Nature, and future developments' (2009) The Information Society, 25(3), 153–158.
[169] Floridi (n 2) (n 4); Floridi, L. *The ethics of information* (Oxford University Press 2013).

points. Furthermore, the approach that Floridi proposes for the governance of digital society aligns with the understanding of a governance broader than ethics, as I proposed for biobanks in the previous chapter – namely, a structure that provides the right conditions to align research and societal interests towards the ethically central issues for most stakeholders. Given that the digital society disrupts the assumptions traditionally held about education, work, health, production, security and so on, we could design and govern it in a way that is not only sustainable but also ethically and societally desirable.[170]

Returning to the focus of this section, digital society is data-driven in almost every sector, as it is in biomedical research. Thus, in the field of biomedical research, decision-making is based on information extracted by data, and this has become possible thanks to the fact that biomedical big data have increased on an unprecedented scale. We can talk about the emergence of a new digital paradigm in this field that has triggered unprecedented change at epistemological, practical and ethical levels. Accordingly, I maintain that any critical analysis of the impact of the digital society on biobank governance should start from an acknowledgement of this paradigm shift in biomedical research and of the dramatic change in how biomedical research is conducted, representing today the state of the art of the research environment in which biobanks operate. In exploring this context, we should bear in mind that biobanks are involved in these epochal changes as supporting infrastructures for translational research and personalised medicine, as explained in Chapter 1.

From an epistemological perspective, it is worth considering that the availability of biomedical big data and big data technologies has produced an unprecedented shift from knowledge-driven science to data-driven science. It can be argued that this enables 'an entirely new epistemological approach for making sense of the world; rather than testing a theory by analysing relevant data, new data analytics seek to gain insights 'born from the data'.[171]

In other words, the principal appeal of the paradigm shift for researchers is the possibility of replacing the observation step – the starting point of traditional scientific methods – with a dataset carefully selected based on the research purpose.

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[170] L. Floridi, L. 'Soft ethics, the governance of the digital and the General Data Protection Regulation' (2018) Philosophical Transactions of the Royal Society A: Mathematical, Physical and Engineering Sciences, *376*(2133), 20180081.

[171] R. Kitchin, 'Big Data, new epistemologies and paradigm shifts' (2014) Big data & society, *1*(1).

However, the literature on the topic is divided when it comes to the scope of this paradigm shift[172] and to defining the real impacts of this digital paradigm in terms of scientific method and knowledge production.[173] For the purposes of this dissertation, I believe that it is sufficient to understand the opportunity offered by the digital paradigm to biomedical research in the following way:

> Data-driven science seeks to hold to the tenets of the scientific method, but is more open to using a hybrid combination of abductive, inductive and deductive approaches to advance the understanding of a phenomenon. It differs from the traditional, experimental deductive design in that it seeks to generate hypotheses and insights 'born from the data' rather than 'born from the theory.[174]

In other words, the focus is not on declaring the end of a theory-centric view of science and seeking a merely empirical and inductive approach that sees the data as the only input for biomedical research. Rather, and this is fundamental to understanding the implications for biobanks, it concerns acknowledging and addressing the consequences of the fact that continuing to use traditional and deductive research designs makes little sense when:

> Technological and methodological advances mean that it is possible to undertake a much richer analysis of data – applying new data analytics and being able to connect together large, disparate data together in ways that were hitherto impossible, and which produce new valuable data and identify and tackle questions in new and exciting ways.[175]

In the transition to practice, these epistemological considerations can be understood in the following way. Biomedical researchers today can rely on accurate data sets from which it is possible to open new lines of research. These data sets typically come from the omics disciplines (e.g. genomics, transcriptomics, proteomics and metabolomics) and biomedical imaging data (e.g. X-ray, CT and PET images). They are supported by new techniques that

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[172] H. Tony, S. Tansley, and K. Tolle, *The Fourth Paradigm. Data-Intensive Scientific Discovery* (Microsoft Research 2009).

[173] S. Leonelli, 'Scientific Research and Big Data' in E. N. Zalta (ed.) *The Stanford Encyclopedia of Philosophy* (Summer 2020 Edition), Available at https://plato.stanford.edu/archives/sum2020/entries/science-big-data/ Accessed 2 March 2022.

[174] Kitchin (no 7).

[175] Ivi, p. 6.

have produced substantial advances in AI technologies for data mining and pattern recognition, and an unprecedented increase in spatial resolution achieved by conventional confocal and super-resolution light microscopy and modern electron microscopes.[176]

Therefore, biomedical researchers are today able to design their research projects starting from the analysis of biomedical datasets to find novel associations between biological entities, identify relevant biomarkers and build elaborate markers of disease and treatments.[177]

Regarding the concrete use of biomedical big data tools and applications in this field, their main role is to provide data repositories, computing infrastructure, and efficient data manipulation tools for investigators to gather and analyse biological information.[178] Luo and colleagues classify big data technological applications into four categories: (1) data storage and retrieval, (2) error identification, (3) data analysis and (4) platform integration deployment and, accordingly, they list the main opportunities that these applications unfold for biomedical research:

> (1) Integrating different sources of information enables clinicians to depict a new view of patient care processes that consider a patient's holistic health status, from genome to behaviour; (2) the availability of novel mobile health technologies facilitates real-time data gathering with more accuracy; (3) the implementation of distributed platforms enables data archiving and analysis, which will further be developed for decision support; and (4) the inclusion of geographical and environmental information may further increase the ability to interpret gathered data and extract new knowledge.[179]

Keeping in mind these considerations, I now move to the analysis of the ethical issues brought by the digital paradigm in biomedical research. Given that data-driven biomedical research can be understood as a combination of 'practices centered on the mass curation

[176] L. Kuhn Cuellar and others, 'A data management infrastructure for the integration of imaging and omics data in life sciences' (2022) BMC bioinformatics, *23*(1), 1–20.
[177] S. Tarazona, L. Balzano-Nogueira & A. Conesa, 'Multiomics data integration in time series experiments' in *Comprehensive Analytical Chemistry* Vol. 82, (Elsevier 2018) 505–532.
[178] M. Mitra, 'Artificial Intelligence in Biomedical Science' (2019) Advances in Bioengineering and Biomedical Science Research 2 1-2. 10.33140/ABBSR.02.04.06.
[179] J. Luo and others, 'Big data application in biomedical research and health care: a literature review', (2016) Biomed Inform Insights: 8 1–10, p. 8.

and processing of personal data',[180] I maintain that two fundamental facts lie at the core of ethical issues: i) biomedical big data are personal data; ii) the main source of ethical problems related to this practice is that those data can be reused and re-purposed multiple times after the collection of human biological samples and the generation of data sets and this makes it impossible to rely on specific informed consent as a guarantee of respect for individual autonomy.

In the first place, biomedical big data are 'personal data' because they are related to identifiable individuals. In addition, these data are considered 'sensitive' and deserving of extra attention and protection during collection, processing and sharing.[181] Unsurprisingly, biomedical big data – understood as a combination of health, genetic and biometric data – are labelled as sensitive under the GDPR.[182] It is important to note that it is precisely the linking of data sets with an individual that gives big data the power to become transformative[183] namely, to make a significant difference in terms of biomedical research progress.

Given the above, it can be argued that the main source of ethical challenges is precisely this fundamental lack of certainty concerning the secondary uses of personal data which is inherent to biomedical big data;[184] that is, the questioning of the privacy, confidentiality and self-determination that have traditionally enabled an individual to exercise control over the use and disclosure of information concerning themselves. Indeed, data-intensive biomedical research involves the re-use and re-purposing of existing biological samples and data sets for research purposes which were not anticipated at the time of the collection of the biospecimens and the generation of the data. Therefore, the ethical concerns arise precisely from the sensitivity of the personal data manipulated and their seemingly limitless potential uses and repurposing, removing the possibility for data subjects to exercise control over the use and disclosure of information concerning themselves.

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[180] B. D. Mittelstadt & L. Floridi, (Eds.) *The ethics of biomedical big data* Vol. 29 (Springer 2016) 1.
[181] S. Slokenberga, 'Setting the Foundations: Individual Rights, Public Interest, Scientific Research and Biobanking' (2021) GDPR and Biobanking, 11–30. doi:10.1007/978-3-030-49388-2_2
[182] Article 4(1) of GDPR defined personal data "any information which are related to an identified or identifiable natural person". Accordingly, the category of personal data is also extended to coded, encrypted and pseudonomysied data which are commonly used for biomedical research purposes. In addition, Article 9 of GDPR establishes special categories that require extra attention defining them "sensitive data": among this sensitive data figures "genetic and biometric data".
[183] G. M Weber, K. D Mandl & I. S. Kohane, 'Finding the missing link for big biomedical data' (2014) Jama, *311*(24), 2479–2480.
[184] I. G. Cohen and others (Eds.) *Big data, health law, and bioethics* (Cambridge University Press 2018).

It is in the light of these considerations that a critical ethical analysis of data-driven biomedical research forces us to reassess certain concepts and issues typically related to traditional research ethics.[185]

At a general level, it is important to acknowledge that the risks for individuals and groups from the re-use or re-purposing of sensitive personal data, or by being affected by the outcomes of the resulting research, must be seen against the needs and goals of biomedical research. Hence, what is at stake from an ethical point of view is the balance between individual and collective interests. That is, researchers need to obtain access to human specimens and data sets to advance biomedical knowledge, a social benefit. Conversely, research participants are asked for access to their body parts and personal data and accept some risks to their well-being and privacy for the sake of others. In the light of this and since many biomedical datasets involve the re-use and re-purposing of records and data from clinical trials, biobank samples and non-medical behavioural data, the protection of data subjects is an ethical priority and must focus on how to implement ethical practices that foster the use of biomedical big data in research while protecting informational privacy and the confidentiality of individuals.

More specifically, the principal ethical but also legal and societal challenges raised by the digital paradigm in biomedical research that will be studied in the remain of this work can be grouped as related to the following issues: i) privacy and data protection; ii) informed consent; iii) ethical oversight.

Privacy and data protection.

Data-driven biomedical research relies primarily on the availability of human biological specimens from which biomedical data are extracted to generate data sets.
Unsurprisingly, this new way of conducting research presents new risks for data subjects or research participants, those to whom the biomedical data belonged before they were collected in various contexts: directly from citizens through eHealth and mHealth apps, clinical trials and biobanks. The principal ethical challenge that the digital paradigm on biomedical research – and, in turn, on biobank governance – is its impact on privacy.[186] This is because all biomedical data are highly sensitive, reflecting an individual's health status

[185] Mittelstadt & Floridi (n 18).
[186] P. Berrang and others, 'Dissecting privacy risks in biomedical data' in *2018 IEEE European Symposium on Security and Privacy (EuroS&P)* (IEEE 2018) 62–76.

and diseases carried. The sensitivity of biomedical data brings additional risk when combined with certain inner features of big data, such as data analytics, data transferability, data interdependency and the links between datasets of different natures.[187] Beyond the technicalities of such complex questions, a number of features of how biomedical research is conducted today under the digital paradigm endanger the right to privacy of individuals. In particular, as a result of the intensive exploitation of datasets and the high likelihood of the re-identification of personal data, anonymisation is no longer able to be guaranteed:

> We have ceased to be isolated pieces of data and have become datasets, stored in different databases that can be combined with the aim of drawing conclusions to improve decision-making; so we have gone from being anonymous to being re-identifiable.[188]

Therefore, in addressing ethical issues, continuous de Lecuona, related to data-driven biomedical research:

> The crux of the matter lies in what kind of personal data are going to be requested, how they are going to be obtained and stored, and how they are going to be processed, whether codified or pseudonymized, who is going to have access, for how long, and what is going to happen with the personal data once the intervention is over. At the same time, the interest is focused on how datasets are going to be combined; for example, those stored in heavily protected electronic medical records with other personal data from other databases outside the health system, which could refer to their owners' patterns of behavior through the analysis of their mobile telephone database, or others, such as health surveys.[189]

The traditional research ethics framework typically seeks to protect and enhance research participants' rights to privacy, confidentiality, and self-determination with respect to the disclosure of their information for research purposes, hence to protect their personal data in order not to cause harm through data misuse and breach of confidentiality. Indeed, the

[187] F. K. Dankar & R. Badji, 'A risk-based framework for biomedical data sharing' (2017) Journal of Biomedical Informatics, *66*, 231–240.
[188] I. De Lecuona Ramírez , 'Guidelines for reviewing health research and innovation projects that use emergent technologies and personal data' (University of Barcelona Editions 2021).

[189] Ivi, p. 64.

potential to re-use and re-purpose personal data – identified as the main trigger of ethical problems in data-driven biomedical research – poses a significant challenge to traditional mechanisms of privacy, confidentiality and data protection. As argued by Lawrence, in the case of data-driven biomedical research 'privacy should be respected because people should be respected';[190] the more research participants feel protected, the more encouraged the public will be to become involved in research and allow their biospecimens and associated personal data to be used.

Once it is understood that protecting participant data is the best way to protect participants in biomedical research, it is important to clarify how research participants can be harmed in the context of data-driven biomedical research, namely the concrete risks that they run while their biological samples and associated data are used in a research project. The wrongful disclosure of genetic or health-related data collected, shared and processed for research purposes may expose research participants and data subjects to 'embarrassment, defamation, stigmatisation, harassment, extortion, identity theft, or financial fraud, or denial of access to health or life insurance, employment, job promotion, or loans'.[191] It is important to understand that these potential harms may take the form of covert forms of discrimination in health-related decision-making, services and opportunities or in the abuse of power against individuals since big data creates a power imbalance between those who hold and apply the data and those who knowingly or unknowingly supply it.

Those risks are pointed out by de Lecuona that warns us that, at a later date, personal data collected for research purposes:

> Could be used for unwanted purposes and give rise to covert discrimination, with profound implications for people's freedom and that of future generations. The possession of personal datasets by third parties, whether private or public initiatives, could affect our rights depending on the uses, giving these third parties extraordinary power over us, a situation that goes unnoticed by the great majority of people.[192]

[190] W. W. Lowrance, *Privacy, confidentiality, and health research* Vol. 20 (Cambridge University Press 2012) 3.
[191] ibid.
[192] Lecuona Ramírez (n 16) 63.

Furthermore, data protection and respect for the right to privacy are essential not only to protect data subjects but also for other stakeholders involved in the research enterprise, since a breach of confidence may also harm researchers and research institutions in terms of negative publicity, litigation or financial losses. As pointed out by Lowrence,

> A breach of confidence can cost months or years of remediating effort by university administrators or clinical or corporate managers and their lawyers and public affairs staff, and a sullied reputation can be a burden for a long time. A research team may be denied access to data or data-collection opportunities, and even a whole line of research may suffer by association.[193]

In such a scenario, it must be acknowledged that the classic model of privacy protection fails to protect research participants' privacy in the digital age.[194] This is in large part due to technical reasons related to the challenges associated with big data analytics. Indeed, from a technical point of view, biomedical research today works with large and complex datasets and many traditional privacy processes cannot handle the scale and velocity required. The ethical counterpart, as argued by Mantelero and Vaciago, is a set of concerns related to 'the way in which big data analytics affect individuals' chances to assume aware decisions about the use of their personal information and affect individuals' expectations of privacy'.[195]

The classic model of privacy protection and the data protection regulations are based on two pillars – the principles of purpose specification and use limitation – and specific consent (informed and freely given) has always been the legal basis for data processing. However, continue the authors, this framework is today challenged by the transformative use of big data:[196]

> Since analytics are designed to extract hidden or unpredictable inferences and correlations from datasets, it becomes difficult to define ex ante the purposes of data processing […] and be compliant with the limitation principle. Therefore, a notice that

[193] Lowrance (n 207) 5.
[194] A. Mantelero (2019) La privacy all'epoca dei Big Data, in V. Cuffaro, R. D'Orazio R. & V. Ricciuto (eds) *I dati personali nel diritto europeo*, Giappichelli, Torino; P. Guarda (2021) *Il regime giuridico dei dati della ricerca scientifica,* Editoriale scientifica.
[195] A. Mantelero, G. Vaciago (2015) Data protection in a big data society. Ideas for a future regulation. Digital Investigation, 15: p. 104.
[196] O. Tene & J. Polonetsky (2011) Privacy in the age of big data: a time for big decisions. *Stan. L. Rev. Online*, *64*, 63.

> explains all the possible uses of data is hard to be given to data subjects at the time of the initial data collection.[197]

Besides the concrete risks related to participants' privacy and the need to implement adequate mechanisms for data protection that better fit the characteristics of data-driven research, it is important to understand that core to an ethical digital society is the need to foster a new awareness about the risks related to the processing of personal data in biomedical research. Our society is defined by a tendency to give away personal data through multiple media without any real concern about protection against unwanted secondary uses. This phenomenon urges a rethink of the data protection framework beyond the individual dimension while the traditional notions of privacy and data protection are primarily based on the model of individual rights.

> The use of massive datasets for social surveillance and predictive purposes in different fields (marketing, employment, social care, etc.) and its potential negative effect, in terms of unfair discrimination […] make it necessary to consider the collective dimension of data protection and, more in general, of the use of data.[198]

In line with this reasoning, I argue that it is important to implement a biomedical research governance ethically committed to ensuring that, if samples and data are collected for a specific purpose, then secondary uses will be in line with that purpose. Therefore, I maintain that data protection in data-driven biomedical research means also protecting research participants' interests against potentially disrupting secondary uses.

Informed consent

Data-driven biomedical research poses a significant challenge to how informed consent has been conceived so far, namely a guarantee of respect for individual autonomy. As observed by Mittelstand and Floridi:

[197] Ibidem. 105-106
[198] Mantelero and Vaciago (n 212) 109

> The adaptation of models and mechanisms of informed consent to biomedical Big Data research has not proven easy. Traditionally, consent is specific which means that individuals agree to undergo a particular procedure or participate in a particular study following in-depth consideration of its merits and risks, assisted by informed medical professionals.[199]

This understanding and function of informed consent is challenged by the possibility of re-using and re-purposing biospecimens and associated personal data in biomedical research, in brief by secondary uses following the moment of collection. Traditional informed consent is not compatible with how research is conducted today. Even before examining the merits and procedural difficulties of collecting truly informed consent faced with the possible re-use of the data for future research purposes – and the much-discussed introduction of different types of consent (i.e. broad, open or blanket consents) that better fit the scope of data-driven research – the problem of consent arises at the level of principles. The philosopher Savulescu provocatively talks about the 'widespread malaise' affecting biomedical ethics today:

> We now have enormous scientific capacity to construct population-level genetic and other databases that could massively enhance knowledge and save and improve lives. But such research cannot be carried out because of 'ethical' obstacles and data protection. […] This problem of large datasets is symptomatic of an obsession with prioritizing consent over all other values.[200]

Despite his polemic tone, the author identifies the heart of the difficulty around informed consent and maintaining its role in data-driven biomedical research. We must acknowledge, indeed, the fact that in the context of data-driven biomedical research we face a crisis of the paramount position of informed consent as a guarantor of the principle of autonomy that consent procedures are committed to protect and that has always been a cornerstone of research ethics.

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[199] Mittelstadt & Floridi (n 18).

[200] J. Savulescu, 'Bioethics: why philosophy is essential for progress' (2015) Journal of Medical Ethics *41*(1), 28–33.

At a concrete level, it can be distinguished between two overarching families of consent in biomedical research, borrowing wording from the vocabulary of data science: opt-in consent and opt-out consent.

The opt-in formula requires explicit consent from the participant before the collection of biological samples and associated data. It, therefore, refers to an affirmative action taken by participants, indicating their consent to be part of a research project and/or allow the collection, processing and sharing of biosamples and associated data. This family of opt-in consent includes different models: classic, broad and open. In classic – or study-specific – consent, the participant consents for a very specific research purpose with a determined objective. Broad consent offers a useful alternative to classic consent, as the participant can consent for an unspecified range of future research subjects, usually following similar lines of research, without the requirement to obtain additional consent as long as the future activities fall within the scope of the broad consent. Finally, in open-ended or blanket consent the participant gives open-ended permission to the use of their biosamples and data without limitations, that is, without the requirement to obtain additional consent for future research.

The opt-out formula (also known as consent by default), in contrast, does not require the participants' consent to be obtained before collecting and processing their biological samples and personal data. Thus, using the opt-out approach means that participants are included in research unless they give their express decision to be excluded at a later date. To date, the employment of such an approach in biomedical research is still under discussion, although it has been proposed as a more practical way to obtain participants' consent in some branches of research.[201]

As anticipated, the transformative use of biomedical big data and the possibility to reuse and repurpose collected biological samples and personal data are the reason why traditional models of informed consent (classic and broad) are increasingly being called into question and losing their normative power. In the rest of this work, I will refer to secondary use as the use in biomedical research of personal data and human biological materials originally collected for a purpose other than the current research purpose. Such possibilities are inherent to the goal of data-driven research and biobanks, since these often collect samples

[201] L. Cardillo and others, 'Patients' perspectives on opt-out consent for observational research: systematic review and focus group' (2018) British Journal of Nursing, *27*(22), 1321–1329; A. Vellinga and others, 'Opt-out as an acceptable method of obtaining consent in medical research: a short report' (2011) BMC medical research methodology, *11*(1), 1–4.

and data prospectively: data sets and stored samples are likely to be re-used and re-purposed in future research that was not foreseen at the time of data generation or sample collection.

I argue that it is around the question of informed consent that the balance between individual and collective interests becomes more pressing. To foster the goals of data-driven biomedical research and maximise the potential contained in biomedical datasets, it is inappropriate and even anachronistic to continue to prioritise informed consent at the expense of other values such as benefit-sharing and the common good. Yet it is mandatory to continue to guarantee the ethical nature of the procedures involved in biomedical research and to protect research participants through appropriate governance mechanisms beyond consent procedures and ethical oversight.

Ethical oversight

Another important ethical issue regards the importance of appropriate oversight mechanisms for this new research endeavour, based on the exploitation of biomedical big data. To operate at full capacity, data-driven biomedical research relies on biobanks and other repositories of biomedical data. The way in which access to biobanks, databases and other digital infrastructures is regulated becomes critical from an ethical point of view.[202] In other words, it is how the oversight mechanisms – mainly ethics committees and their criteria for the assessment of research projects – are designed and implemented that determine the ethical balance between the interests of research and individual rights. As observed by Mittelstand and Floridi, given that ethics committees increasingly manage access to biomedical big data resources, it is 'in deciding who is given access to the data, and in what format, […] [that oversight] bodies are trusted to protect and balance the interests of individual data subjects, the scientific community, commercial actors and the general public'.[203]

Furthermore, to guarantee that the oversight system of biomedical research provides an adequate response to the emergence of the digital paradigm, we need to adapt the professional responsibilities of researchers and RECs involved in the collection, sharing,

[202] M. Shabani, B. M. Knoppers & P. Borry, 'From the principles of genomic data sharing to the practices of data access committees' (2015) EMBO molecular medicine, *7*(5), 507–509; M. Shabani and others, 'Oversight of genomic data sharing: What roles for ethics and data Access Committees?' (2017) Biopreserv Biobank;15:469–474.
[203] Mittelstadt & Floridi (n 18).

access to and analysis of biomedical data. On the one hand, universities need to 'seek to educate researchers on ethical issues that can arise when conducting data-driven research' and, specifically, that 'researchers would benefit from training on identifying issues of ethics or completing ethics self-assessment forms, particularly if they are responsible for submitting projects for review',[204] while, on the other, RECs need to fill the lack of an effective body and the necessary skills to review research projects in this new context.
In the face of the new challenges, the RECs' mandate – to regulate human subject research by ensuring respect for human rights and that scientific and social interests do not prevail over research participants' rights – risks to fall behind the demands of data-intensive research.[205]

The new research methods and technological developments that are currently challenging the job of the RECs were listed by Ferretti and colleagues in 2021 as follows:

> First, they challenge traditional research principles such as data privacy, informed consent, scientific validity of research, risk assessment, and distribution of benefits. Second, they introduce new epistemic challenges related to the assessment of scientific validity, technological reliability, accountability, fairness, and transparency. Finally, they challenge the very notion of human participants in research, as they enable retrospective data processing without physical interaction with research participants.[206]

Once we have understood that the current oversight mechanism is not fit for purpose to assess the methodological, ethical, legal and societal issues of data-driven biomedical research, it becomes imperative to find a way to adjust and improve RECs if we want such oversight bodies to continue to carry out their fundamental role as guarantors of human rights and participant interests in the context of biomedical research as I have described in Chapter 1. Accordingly, RECs should be improved at several levels to enable them to adequately address and overcome these challenges. The direction and the spaces of implementation have been identified and suggested by scholars. De Lecuona, in her

[204] A. Ferretti and others, 'Ethics review of big data research: What should stay and what should be reformed?' (2021) BMC medical ethics, *22*(1), 1–13, p. 9.

[205] E. Vayena and others, 'Elements of a new ethical framework for big data research' (2016) Washington and Lee Law Review Online, 72(3).
[206] A. Ferretti and others (n 58) 'What should stay'.

proposed guidelines and requirements for the evaluation of big data research projects in health, notes that it is necessary to require REC members to undertake continuous training and updating on big data and data protection, to include data scientists in such committees, to abandon obsolete concepts that generate false security, such as anonymisation, and to demand explanations of researchers on the possibility of data re-identification.[207]

Similarly, Ferretti and colleagues recommend that RECs adapt their membership to include the necessary expertise to address the research needs of the future; that RECs accept external experts' consultations and consider training in big data technical features as well as big data ethics; the need for transparent engagement among stakeholders, which requires ERCs to involve both researchers and data subjects in the assessment of big data research.[208] Finally, there is a need to acknowledge the existing space for coordinated and complementary support action from other forms of oversight.

On the same lines, the Observatory of Bioethics and Law, at the University of Barcelona, has stated that:

> There is thus an urgent need for them to become digitally literate, because of the responsibility these bodies have with regard to the protection of the rights of those involved in processes of research and innovation, including freedom and research, together with other basic rights such as the privacy and the confidentiality of personal data. RECs must be able to identify potential problems and conflicts of interest that may arise in relation to the use of personal data, and what information to request from project leaders, in order to guarantee the protection of individuals' rights.[209]

Having acknowledged the importance of an adequate ethical oversight system that allows the composition and skills of REC members to be altered to keep pace with the new ethical challenges brought by the digital paradigm, I argue that we cannot be limited to a model of governance based on ethical oversights. Indeed, to ensure the adequate protection of research participants in data-driven biomedical research – including biobank participants –

[207] I. de Lecuona, (n 63) 'Evaluación de los aspectos metodológicos'.
[208] A. Ferretti and others (n 58) 'What should stay'.
[209] Lecuona Ramírez (n 16) 67.

we must implement a model of governance that is broader than an ethical oversight of practices.

2.1. The conceptual limits of traditional research ethics

The paradigm shift in biomedical research triggered by the digital society has brought multiple changes at many different levels; consequently, an update of the ethical apparatus is required. Indeed, it is evident that the framework identified as 'ethics of biomedical research' over the past 70 years or so was developed to manage problems and concerns related to the historical abuses of research participants in many biomedical fields during World War II and over the past century.

Updated ethical guidance in the light of progress in biomedical research is crucial if we want to continue to protect research participants' rights dignity, integrity, self-determination and privacy. Although data-driven biomedical research involves no direct relationship between researchers and participants and causes no potential physical harm – previously two of the main areas of concern in traditional research ethics – we have to remember that biomedical research is always potentially harmful if not conducted ethically. In the face of inadequate ethical standards, research participants and, in turn, society will always be in danger.

At the same time, however, care must be taken that ethical standards take account of the digital paradigm. If not, we run the risk of continuing to adopt a precautionary approach – based on how biomedical research used to run – and maintaining a focus on specific informed consent and other ethical dogmas at the expense of other priorities.

The possible harms that may occur as a result of participation in data-driven biomedical research 'are of a different nature to those incurred in the course of clinical research that involves direct bodily intervention such as administering a new drug or procedure and feature a different balance and distribution of risk against the potential benefits.[210]

[210] Chan, S. 'Bioethics in the big data era: health care and beyond' (2017) Revista de Bioética y Derecho, (41), 3–32, p.13.

Given the above considerations, I will compare the traditional framework of research ethics with the new context of data-driven biomedical research, to outline spaces for the implementation of an adequate and updated ethical framework for biobank governance.

Firstly, it is important to understand the change in the concept and role of research participants at the turn of the paradigm shift in data-driven biomedical research. Before the digital age, research participants were patients or healthy volunteers who decided to become involved in clinical trials or other biomedical research projects by making available their bodies, or body tissues, and their health-related information. Today, however, a research participant is understood as a person from whom data and samples have been collected and is often called the 'data subject'. It is in this new understanding that biobank participants are included in the category of research participants. Inevitably, the way in which data-driven biomedical research is conducted, along with how participation in research has changed, has resulted in a redefinition of the risks associated with participation. Therefore, a revision of the existing research ethical guidelines is required if we are not to risk using an ethical framework inadequate for the protection of research participants.

At stake here is the (re) establishment of ethical values and principles in the face of the common perception that biomedical research can represent a threat to human rights and freedoms. I refer to concerns that have always existed in relation to participants' rights to integrity, privacy and protection against discrimination but that today may be exacerbated by the characteristics of biomedical big data and the digital society, creating new ways in which privacy can be infringed, and thus new harms to which people may be exposed when participating in a research project or biobank.

The traditional framework of research ethics was essentially based on the clinical trial paradigm that focused on the protection of the participant against various, but predominantly physical, harms. It was based on the bioethical principles of respect for autonomy, beneficence, non-maleficence and justice conveyed by the reference bioethical texts and documents (described in Chapter 1) that aimed 'to minimize the possibility of exploitation by ensuring that research subjects are not merely used but are treated with respect while they contribute to the social good'.[211]

[211] ibid.

It is worth noting here the paternalistic approach of this ethical framework that, on one side, sees the research participant as a passive subject to be protected and, on the other, the unquestionable power of medicine and its operators. In line with such an approach, the actors considered to be at the core of the research process in this framework were the promoters, researchers, health authorities and pharmaceutical industry.

Finally, the foundations of the research ethics paradigm were laid in a context where the principles of autonomy and informed consent were considered an absolute guarantee of participant protection for every single intervention and this kind of participation included only limited access to and processing of personal information.

Against this scenario, we can compare the situation faced today in the digital society. As shown above, how biomedical research is conducted today has completely changed and, despite some new declarations and regulations,[212] there is a widespread lack of understanding of the digital paradigm at different levels.[213] First, those involved in the research enterprise may also come from sectors traditionally unrelated to biomedicine, such as biotech start-ups, investment funds and independent researchers. In addition, a strong dependence on informatics and biotechnologies must be acknowledged, both in the public and private sectors.

On the side of research participants, however, the phenomenon of collecting and sharing genetic and health-related data provided directly by individuals through ICT (e.g. health apps, wearable mobile technologies, direct-to-consumers genetic tests) has definitively cast patients and public as active actors, managing their participation and in co-operation in research projects.[214] The concept of meaningful participation in the context of data-driven biomedical research has been widely discussed because it does not stop at having one's data included, yet other expectations about the personal and public benefits of research and

[212] World Medical Association. 'World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects' (last version 27 Nov 2013) JAMA 310(20):2191–4. doi: 10.1001/jama;
Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (General Data Protection Regulation). Available at: https://gdpr-info.eu/ [Accessed 21 February 2022].
[213] I. de Lecuona, 'Evaluación de los aspectos metodológicos, éticos, legales y sociales de proyectos de investigación en salud con datos masivos' (big data) (2019). Gaceta Sanitaria, *32*, 576–578.
[214] A. Buyx and others, 'Every participant is a PI. Citizen science and participatory governance in population studies' (2017) International Journal of Epidemiology, *46*(2), 377–384; J. Kaye and others, From patients to partners: participant-centric initiatives in biomedical research (2012) Nature Reviews Genetics, *13*(5), 371–376.

who controls the research agenda can be considered. The rhetoric of 'citizen science' has been invoked by both private and public health-data initiatives to promote participation, either by increasing the desirability of the product or by appealing to individuals' sense of civic duty.[215]

Secondly, the notion that anonymisation can guarantee privacy protection in biometrical and genetic data in biomedical research is dead.[216] In a society where data accumulation occurs by default, we are facing the default re-identification of personal data from the moment that computer engineering techniques make it possible to re-connect previously anonymised or codified personal data to an individual, because the utility of data in biomedical research depends on being able to link it to other – genomic, demographic and health – information about that individual which in turn increases the possibility of re-identification.[217] In this context, transparency and protection against discrimination should be considered as priorities over the principles of autonomy and informed consent, to address the savage capitalism of data in which access to huge volumes of personal data and potential profiling are taken for granted.[218] The ethical challenge here is to understand how to protect research participants and citizens from data exploitation and ensure that the benefit derived from this new form of business will be shared between all the stakeholders.[219] Following Chan's argument, in conceptualising an updated research ethics framework for biomedical research in the digital society, the focus should not be on 'What research cannot be done with my data?' but rather 'What else is being done with it?' intended as a focus on protection against unwanted secondary uses and 'What research can and should be done in order to achieve social benefit?' intended as a way to align research governance with societal interests.[220]

This consideration leads us to introduce another important feature of the context in which biomedical research is conducted today: its proximity to values and logic that derive from the market. Indeed, the global data-driven economy stimulates new health and wellness business models that are fed by personal data (e.g. health, genetic, lifestyle and behavioural

[215] S. Jasanoff, 'Technologies of Humility: Citizen Participation in Governing Science' (2003) *Minerva* **41,** 223–244.
[216] M. Gymrek and others, 'Identifying personal genomes by surname inference' (2013) *Science*, *339*(6117), 321–324.Yaniv Erlich and others, 'Redefining genomic privacy: trust and empowerment' (2014) *PLoS biology* 12, no. 11, e1001983.
[217] Chan (n 33) 13.
[218] T. Sharon, 'When digital health meets digital capitalism, how many common goods are at stake?' (2018) Big Data & Society, *5*(2), 2053951718819032.
[219] A. Bedeker and others, 'A framework for the promotion of ethical benefit sharing in health research' (2022) BMJ Global Health, *7*(2), e008096.
[220] Chan (n 33) 13, 23.

information). Unsurprisingly, these business models are making their way into biomedical research in the pursuit of financial gain over the commercialisation and exploitation of human biological samples and associated health data as we will examine in the second part of this chapter.[221]

To conclude, from the above comparison between the traditional ethical framework for the protection of research participants and the evolution of the field of biomedical research in the digital age, the limits of the current framework are revealed. In my opinion, these also help to identify the following gaps in the implementation of ethical coverage. First, there is a need to consider the evolution of the role of research participants from passive actors simply needing protection from physical harm and abuse of power to active participants who decide to contribute their samples and data to the progress of research. Secondly, we must recognise that traditional forms of informed consent do not cover the ethical concerns related to secondary uses and their associated risks for research participants. Thirdly, anonymisation is not a reliable mechanism to protect the right to privacy of participants in face of the new potential to identify previously de-identified samples and data. Finally, the commercialisation and exploitation of genetic and health-related data – characteristic of the digital era – are not adequately covered by traditional ethical frameworks.

2.2. Ethics of biobanking: the evolution of ELSI

In this paragraph I address the novel ethical implications brought by the digital paradigm to biobanks. Indeed, the emergence of data-driven biomedical research has resulted also in important changes in the collection, storage and use of biobank samples and associated data. The importance of biobanks in providing biomedical researchers with samples from which data can be extracted, and annotated datasets on which to base new hypotheses and lines of enquiry, is now clear. Unsurprisingly, the limits of the traditional ethical framework's ability to address novel ethical issues in biomedical research also extends to the field of biobanks, leading us to question whether pivotal principles and applications now provide adequate ethical coverage for biobanking practices.

[221] K. Evers, J. Forsberg & M. Hansson, 'Commercialisation of biobanks' (2012) Biopreservation and biobanking, *10*(1), 45–47.

I will approach the ethics of biobanking through an analysis and discussion of the ELSI usually associated with biobanks with a particular focus on their evolution with the paradigm shift in biomedical research.

The ethics of biobanking can be understood as an effort to understand and a normative guiding of the function of biobanks in the best direction, attempting to draw a line between what biobanks should and should not do. It is interesting to question why biobanks are the subject of such ethical reflection. Cordell conceptualises the biobank itself as an ethical subject, arguing that 'at stake as subjects in the key ethical questions of biobanking are the primary subjects of ethics and politics, namely the individual and the society'.[222] Indeed, if at a first glance it may seem that the focus of biobank ethics is individual and in particular participants' rights and interests in relation to, for example, privacy, autonomy, dignity and confidentiality, the author observes that 'ethical concerns of biobanking also extend to socio-political interests, goods and benefits—such as public health, the well-being of future generations and even, most generally, scientific knowledge and progress'.[223]

Bearing this premise in mind, ethical concerns in biobanks can be associated with two types of problem. The first corresponds to the question posed by Hansson: 'Does biobank research imply new ethical challenges' *per se*?[224] As a relatively new research practice, it can be said that biobanking has brought unprecedent ethical dilemmas and debate to the field of bioethics, challenging and testing traditional legal concepts, governance provisions and bioethical principles.[225] The major moral concerns are primarily related to characteristic features of biobanks – the prospective collection of samples and associated personal data with the inherent potential to reuse and repurpose them multiple times. Hansson divides them in three groups:

> (i) the selection of appropriate information and consent procedures for different research protocols, (ii) the protection of confidentiality of those who submit tissue material or personal information while still facilitating important research, and (iii) how to handle research results or incidental findings that is of potential interest to the donors or to their genetic relatives.

[222] S. Cordell (2011) The biobank as an ethical subject. *Health care analysis*, *19*(3), p. 283.
[223] Ibidem.
[224] M.G. Hansson (2009) Ethics and biobanks. *British Journal of Cancer*, *100*(1), 8–12.
[225] S.M. Gibbons & J. Kaye (2007) Governing genetic databases: collection, storage and use. *King's Law Journal*, *18*(2), 201–208.

The second set of problems regards the question 'Does data-driven biomedical research imply new ethical challenges for biobanks?' This implies the scope of a new layer of issues added by the emergence of the digital paradigm in biomedical research in detecting both the limits of the traditional ethical framework in the field of biobanking and the concrete ethical concerns that an effective model of biobank governance in the digital society has to face.

The scientific literature on the topic of ethics of biobanking merges with the topic of biobanks' ELSI. This is because as observed by Walker and Morrissey in the context of the Human Genome Project, ethics research within an ELSI framework can be considered a subset of bioethics, since ELSI questions are directly concerned with advances in technology, science and medicine relating to human genomics.[226] The same assumption could apply to biobanks, and this is in line with the understanding of bioethics that I defend in this dissertation. For the sake of this work, I maintain that, although they are closely interrelated, ethics stands out from legal and social considerations in embodying both the background and the potential answer to many issues at stake. Therefore, the primary role of ethics in the context of research biobanks is that of constant engagement in the assessment of actions, motivations, decisions and practices in order to formulate and support solutions.

However, it is important to note that ethical, legal and societal issues are interdependent and, for this reason, need to be addressed through a multidisciplinary approach. In particular, the interweaving of the issues (and their respective disciplines) is seen in the ethical challenges raised by large-scale biobanks and their activities, the legal requirements in response to those ethical issues, and the way in which social forces shape how research projects are constructed and biobank governance is conceived. For this reason, an exhaustive ELSI approach to biobanks should engage a range of scholars, encompassing academic scientists, economists, social scientists, bioethicists and policymakers, which may be easier said than done. For the reasons outlined in the Introduction, this dissertation focuses primarily on ethics, and in particular bioethics.

Coming to the heart of the matter, I now analyse and discuss the core ethical concerns in biobanks and the emerging trends in the scientific debate on biobanks' ELSI. The biobank

[226] R. L. Walker & C. Morrissey, 'Bioethics methods in the ethical, legal, and social implications of the human genome project literature' (2014) Bioethics, *28*(9), 481–490.

field seems to be characterised by multiple ethical tensions and seemingly intractable conflicts:[227] first, the tension between the goals, methods and routes of research progress and the rights of the individuals or groups involved in research biobanks. As observed by Cordell, the discussion on the ethics of biobanks has tended to develop in broader ethical and political terms of 'balancing the rights of individual participants with the "greater good"; or the privacy and autonomy of participants with the "long term health" of a society or the general public and the "public interest" pursued by biobank research'. Secondly, biobanking practices involves a re-examination, even a re-conceptualisation, of the basic principles of biomedical research ethics. To take one example, the paramount position of informed consent as a guarantor of individual autonomy needs now to meet the particular features of biobanks that prospectively collect biospecimens and associated data. This raises the difficulty of providing adequate information to participants at the point of sample and data collection while raising awareness of unforeseen research studies that could be carried out in the future using those samples and data. Thirdly, since biobanks are not detached from the social and economic context, there is the difficulty in protecting the non-commercial use of human body and its parts with the growing role of commercial biobanks. Indeed, although the majority of public biobanks are built on not-for-profit principles, they have to remain financially sustainable over time. This brief overview gives a glimpse into how ethics permeates the debate on biobank governance on many levels and from multiple perspectives.

Moving to a thorough description of the specific issues raised through a review of the literature on ELSI in biobanks, the main papers on this topic can be divided into two blocks: those published before and after 2010. The majority of those in the first block discuss issues and challenges related to biobanks from the 1990s to 2010, an era of infrastructural transition for biobanks in which they were transformed from personal medical repositories to systematic and organised collections. The later studies, published from 2010 to the present day, instead review the new challenges brought by advances in molecular medicine and genomics but also by a paradigm shift in biomedical research driven by big data. Another important turning point for ELSI in biobanking, as we will explore later in more detail, was the implementation of the new GDPR in 2016 and the new challenges related to the protection of personal data.

[227] A. Cambon-Thomsen, 'The social and ethical issues of post-genomic human biobanks' (2004) Nature Reviews Genetics, *5*(11), 866–873.

Many proposals have been made to classify ELSI in research biobanks. I will now present four different ways in which ELSI has been analysed and discussed by some of the most representative studies on the topic published within the selected timeframe.

In one of the first and most-cited analyses of ethical and legal frameworks for human biobanks, Cambon-Thomsen and colleagues identified three principal recurring trends: informed consent, confidentiality and the sharing of data and results. Each of these three categories encompasses controversial issues, including secondary uses of samples and data, public engagement and trust (i.e. the overall relationship between participants, biobankers, the general public and finding mechanisms for building trust), the dissemination of results (i.e. the return of results to participants, confidentiality in order to protect participants from the risk of stigmatisation and discrimination), the commercialisation of biobank resources and benefit-sharing across society.[228]

In the introduction to their monograph on the ethics of research biobanking, published in 2009, Solbakk and colleagues effectively identify four clusters of issues and pose several questions that help to explore each of them. They are listed from the most discussed to the least explored. The first cluster collates those issues concerned with how biological materials are entered into biobanks – finding answers to questions around what kind of consent should be given by participants and how to implement participants' rights, such as the right to retain, withdraw from, or renew consent and other opt-in/opt-out systems. The cluster also addresses questions about the conditions under which materials collected by a biobank can be converted into research materials and the secondary uses of samples and data for future research.

The second cluster includes those issues concerning research biobanks as institutions, questioning what kind of institution a biobank is and how to regulate its relationship with social stakeholders.

The third group involves issues concerning the conditions under which researchers can access materials in the biobank. The challenges here range from problems concerning the ownership of biological materials and intellectual property to rules for access to biobank collections and questions of prioritisation among a number of competing research projects.

[228] A. Cambon-Thomsen, E. Rial-Sebbag & B. M. Knoppers, 'Trends in ethical and legal frameworks for the use of human biobanks' (2007) European Respiratory Journal, *30*(2), 373–382.

The final group of issues relates to the information collected and stored, highlighting challenges around access rights, disclosure, confidentiality and data security; in other words, the answer to questions about the best way to protect participants' personal data.[229]

An original way of framing the question has been proposed by Chalmers and co-authors who proposed a framework that divides ELSI according to the stages (waves) of the historical evolution of biobanks as research infrastructures.

The first wave, which coincides with the establishment of the first biobanks, saw experts in the biobank field wondering about management and governance frameworks that could address issues of consent, privacy, governance and security but also engage in the controversial debate on public and private good and benefit-sharing. The second wave corresponds to the initiation of collaborations between biobanks, and the consequent creation of international networks. Attempts to achieve standardisation in biobank practice have brought difficulties in reaching a harmonisation of rules on data confidentiality, access policy, etc.

The third wave brought questions around the sustainability of biobank activities, both at the economic level and in terms of retaining the support of society, raising concerns related to the commercialisation of biobank resources and how to maintain public trust.

Finally, the authors depict future scenarios for biobanks, anticipating that in the fourth wave biobanks will continue to face a number of existing challenges: whether or not to broaden the scope of consent, exploring appropriate ways to enhance participants' involvement, and maintaining public trust in research biobanks in an increasingly commercialised research environment.[230]

More recently, Goisauf and colleagues have divided ELSI in research biobanks into three areas of concern resulting from the latest advances in molecular research and genomics: first, the question of transparency – which is increasingly demanded by participants and other stakeholders regarding the use and sharing of health data for research; second, the increasing interest of participants in becoming partners or even stakeholders in biobanks' activities; third, the controversial issue of developing partnerships between publicly funded

[229] J. H. Solbakk, S. Holm & B. Hofmann (Eds.) *The ethics of research biobanking* (Springer 2009) 115.

[230] D. Chalmers and others, 'Has the biobank bubble burst? Withstanding the challenges for sustainable biobanking in the digital era' (2016) BMC medical ethics, *17*(1), 1–14.

biobanks and industrial actors 'such as pharmaceutical companies and biotechnology start-ups, to accelerate research discovery and promote the advancement of personalised medicine'.[231]

To sum up, by pulling together these different interpretations and considering the evolution of biobanking over time, we can draw several considerations on biobanks' ELSI. First, some issues persist from the early days and can be considered as inherent to biobanks. I refer here to informed consent, the protection of participants' privacy and confidentiality, and the regulation of secondary uses of collected samples and data. Secondly, it appears clear that informed consent is the most debated issue over time and that debate on the best model for consent has saturated the literature on biobanks. Thirdly, a new set of issues has emerged to be addressed in accordance with the evolution of society and new research assets: transparency, participation, public engagement, commercialisation and trust. In particular, among the emerging trends of ELSI in biobanking, that which stands out is the need to replace existing ethical principles such as specific consent by implementing a model of governance that includes ethical tools and concrete mechanisms to ensure that biosamples and data are used appropriately and that the rights of biobank participants are adequately respected and protected.

Accordingly, I argue that this analysis of the evolution of the ELSI of biobanking set alongside the limits of research ethics outlined above demonstrates that the traditional research ethical framework is unfit to provide adequate protection to biobank participants against the risks introduced by new ways of conducting research and must be updated. This is primarily because the application of the research ethical framework to biobank governance manifests limits, some conceptual and others related to the specific nature of biobank practices, that are simply accentuated by features of the digital paradigm.

Firstly, in conceptual terms, research governance based on the traditional ethics framework 'is parochial, being based around national boundaries and designed for one research project, one researcher and one jurisdiction' and is 'intended to protect individual research participants from physical harm rather than informational harm',[232] focused on ensuring that research ethics committees protect research participants' interests and that informed

[231] M. Goisauf and others, 'Data in question: A survey of European biobank professionals on ethical, legal and societal challenges of biobank research' (2019) PloS One, *14*(9), e0221496.
[232] J. Kaye, 'From single biobanks to international networks: developing e-governance' (2011) Human Genetics, *130*(3), 377–382.

consent procedures are implemented and respected. In contrast, effective governance of data-driven biomedical research must evolve in accordance with new ways of conducting research based on flows of data and international sharing, and must address the ethical, legal and societal issues related to the re-use and re-purposing of biospecimens and personal data stores in biobanks and databases.

In the following section, I identify and discuss the reasons why the application of standard ethical principles to protect research participants may be inappropriate for biobanks. In the first place, I refer here to the impossibility for biobanks to rely on specific informed consent as a guarantee of the protection of participants' autonomy,[233] a feature that ELSI related to the possibility to secondary uses and purposes in data-driven biomedical research only exacerbate. The focus on future research and fostering the goals of data-driven biomedical research – rather than on the direct impact of the research on the individual – along with the unique feature of biobanks, namely that samples and data are collected prospectively, have led to major consequences in informed consent procedures. Specifically, biobank participants are often asked to consent to unspecified research purposes and face a lack of adequate information, resulting in a loss of autonomy and control over their own samples and data. Accordingly, the traditional meaning and value of informed consent – based on the ideal of informed, free, prior and explicit consent –cannot accommodate these broad and future consents that are more appropriate for the scope of biobanks, and this undermines the power of the research ethics framework to protect biobank participants.

From a philosophical point of view, the arguments against the use of traditional informed consent in biobanks can be divided into two groups, as explained by Sanchini and colleagues.[234]

> The most widely known objection to the use of traditional informed consent in biobanks relates to the requirement of providing participants with full information about the research projects in which the specimens will be utilized. However, since at the time of collection it is impossible to foresee the future role of tissue samples in

[233] M. G. Hansson and others, 'Should donors be allowed to give broad consent to future biobank research?' (2006) The Lancet Oncology, *7*(3), 266–269;
J. Allen & B McNamara, 'Reconsidering the value of consent in biobank research' (2011) Bioethics, *25*(3), 155–66. M. Sheehan, 'Can broad consent be informed consent?' (2011) Public Health Ethics, *4*(3), 226–235. B. Hofmann, J.H. Solbakk & S. Holm (2009) Consent to Biobank Research: One Size Fits All? in: J.H. Solbakk, S. Holm & B. Hofmann (eds) *The Ethics of Research Biobanking,* Springer US, 3–23.
[234] V. Sanchini, G. Bonizzi, D. Disalvatore, M. Monturano, S. Pece, G. Viale ... & G. Boniolo (2016). A trust-based pact in research biobanks. From theory to practice, *Bioethics*, *30*(4), 260–271, p. 261.

> research, the provision of full information prior to signing of the consent is unfeasible. Therefore, the very concept of an IC for research biobanks as a means to provide the prospective participant with 'full information' seems inconsistent.[235]

Moreover, the discussion of the most appropriate type of consent for biobanking in the range of the opt-in models (specific, broad, blanket) and of the information that renders consent 'informed' must also take into consideration the fact that biobanks are human genetic and biological databases and that the personal data that they collect, store and give to researchers are personal for more than the individual who has agreed to participate with their samples and data: the samples and data collected, stored and shared in and by a biobank contain information about connected individuals:

> These may be consanguineous relations or cohorts associated by genetics, heredity, age, lifestyle, gender and so on, or whole populations. Thus, genetic information given by donors is typically about a number of persons and the uses to which it may be put are not specifiable in a way that preserves individual 'autonomy' as informed consent is supposed to do.[236]

This acknowledgement supports the second group of objections to the use of traditional informed consent for biobanking. That is, the conception of autonomy underlying traditional informed consent is based on the idea that a decision is legitimate as long as it is the result of an informed and voluntary choice by a competent person. Such an idea seems to be very distant from the concept of autonomy tacitly accepted within the context of biobanks. Here, 'the participant is considered as an autonomous agent even if he/she decides to exercise his/her right of not knowing the information deriving from the use of his/her biological material. This means to endorse a different concept of autonomy, mainly based on the act of choosing'.[237]

On the basis of these considerations it is clear that, to overcome the limitations of traditional informed consent in biobanks, an adequate model of biobank governance needs to place greater reliance on broad consent for the future use of samples and data in order to match

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[235] Ibidem.
[236] Cordell (n221) 284
[237] Sanchini, V., Bonizzi, G., Disalvatore, D., Monturano, M., Pece, S., Viale, G., ... & Boniolo, G. (2016). A trust-based pact in research biobanks. From theory to practice. *Bioethics*, *30*(4), 260-271. P. 261

the scope of biobanking but, at the same time, provide appropriate ethical safeguards and mechanisms to protect biobank participants to ensure that biobank samples and data are used appropriately regardless of the information that biobank personnel have been able to provide to the individual at the moment of collection.

Secondly, the issues outlined above regarding traditional informed consent also apply to the concept of privacy, which needs to be reassessed in relation to biobanking in data-driven biomedical research[238] primarily because the intrinsic purpose of biobanking is the sharing of human biological samples and personal data with external researchers. Therefore, in the context of biobanks, the right to privacy and confidentiality of the participant is waived in order to make research possible.[239]

If the physical risks to biobank participants are relatively minor – and virtually non-existent when the research concerns previously stored biospecimens – the risks related to the privacy of biobank participants merit special attention in the effort to conceptualise an adequate governance model.

In the past – that is, in the analogue era – discussions related to the right to privacy and the confidentiality of personal information, a pillar of research ethics, were easily resolved by reference to anonymisation: if participants' samples and data are anonymised, their privacy is protected. Today, although research – including that conducted with biobank resources – is most often conducted with de-identified information,[240] reidentification is always possible[241] and the notion of anonymisation has ceased to be the best option for the protection and promotion of the participants' interests. As explained by Aicardi and colleagues:

> Not only is the anonymity of data and material highly context-dependent, but data and material that are anonymized today may no longer be anonymous in the context of tomorrow's technologies and data resources. Whatever is contained in a health database or a biobank may be anonymized and non-identifiable at the time it is set

[238] D. Pullman, H. Etchegary, K. Gallagher, K. Hodgkinson, M. Keough, D. Morgan & C. Street (2012). Personal privacy, public benefits, and biobanks: a conjoint analysis of policy priorities and public perceptions. *Genetics in medicine*, *14*(2), 229–235.
[239] L. Ø. Ursin (2008). Biobank research and the right to privacy. *Theoretical medicine and bioethics*, *29*(4), 267–285.
[240] R. Chevrier, V. Foufi, C. Gaudet-Blavignac, C. Robert, A. & Lovis, C. (2019). Use and understanding of anonymization and de-identification in the biomedical literature: scoping review. *Journal of Medical Internet Research*, *21*(5), e13484.
[241] This means that data can be linked again to identify a specific individual.

up, but this may not remain so over time, especially when data from the database or biobank are linked with other data sets.[242]

Therefore, when discussing privacy in biobanking, 'the primary concern is that biobank research involves collecting sensitive health information about the participants and updating this through linkage to other medical and nonmedical registers'.[243] In other words, to protect biobank participants, there needs to be protection against infringements of their privacy.

Thirdly, the limits of the traditional research ethics framework in the context of biobanks extend to decisions on who can access biobanked samples and data. To address this issue, each biobank relies on an ethical committee (internal or external) responsible for assessing requests from researchers and research centres for biospecimens and datasets. To inform the decision-making process, a set of access arrangements is established by each biobank to provide ethical guidelines and practical procedures for the handling of requests from external researchers for access to the biobank collection.

As I have argued above regarding informed consent and privacy, the traditional concept of the ethical review of research projects may be inadequate in biobanking. It is possible to distinguish between the levels of difficulty that an ethical oversight body can experience when dealing with biobanks. The first relates to the connatural ELSI of biobanks – the extent of broad consent for secondary uses, incidental findings or the return of results to the biobanks and to participants – that are not yet adequately reflected in the guidelines and challenge the decision-making process. The second level relates rather to those ethical concerns that arise with the sharing of genetic and health-related data in the face of broad consent. The latest literature on this specific topic,[244] namely, the oversight of genetic and genomic data sharing, has focused the debate on the need to implement adequate

[242] C. Aicardi and others, 'Emerging ethical issues regarding digital health data. On the world medical association draft declaration on ethical considerations regarding health databases and biobanks' (2016) Croatian Medical Journal, *57*(2), 210.
[243] L. Ø. Ursin (2008). Biobank research and the right to privacy. *Theoretical medicine and bioethics*, *29*(4), 267–285, p. 268.
[244] M. Shabani, E. S. Dove, M. Murtagh, B. M. Knoppers & P. Borry (2017). Oversight of genomic data sharing: what roles for ethics and data access committees? *Biopreservation and biobanking*, *15*(5), 469–474; E. S. Dove, D. Townend, E. M. Meslin, M. Bobrow, K. Littler, D. Nicol, ... & B. M. Knoppers (2016). Ethics review for international data-intensive research. *Science*, *351*(6280), 1399–1400; J. Kaye, L. Briceño Moraia, C. Mitchell, J. Bell, J. A. Bovenberg, A. M. Tassé & B. M. Knoppers (2016). Access governance for biobanks: the case of the bioshare-eu cohorts. *Biopreservation and Biobanking*, *14*(3), 201–206.

governance mechanisms to manage access to biobank data and their importance in growing data-driven biomedical research. Biobanks, like other research infrastructures, should better define access arrangements that help to overcome undeveloped data access criteria, the lack of sufficient oversight mechanisms and the need for fairness and transparency in terms of access decisions when addressing data sharing.

Faced with this new level of issues, I maintain that the ethical framework and criteria that traditional ethics of biomedical research provide to oversight bodies is inadequate. In particular, in the case of biobanks, there is a need to rethink whether governance mechanisms adequately monitor and manage access to data especially in the light of new concerns about the privacy and confidentiality of personal information. The goal of ethical oversight in biobanks in the context of data-intensive research should be to grant access to qualified researchers for a set of appropriate uses.

3. The commodification of human biological samples and personal data in the digital society

This work aims to conceptualise and propose a governance model for biobanks, which are considered key tools in fostering research and innovation in the digital age.

How biomedical research is developed from biobanks and the way in which its goals are pursued are not neutral. Rather, they result from scientific, political and economic commitments and decisions, strongly influenced by prevailing social trends. Below, I argue that one of the greatest challenges for biobank governance today is the irruption of market logic in a research context, leading to a tendency towards the commodification of human biological samples and datasets. This trend is in line with the goals of the digital society and data-driven economy pursued by the European Union and its Member States, which stimulate health and care business models fed by health-related personal data. Therefore, while the core mission of biobanks lies in collecting, organising and providing high-quality biospecimens and associated personal data to the scientific community for translational research and personalised medicine, it is worth questioning the logic and influence of the

economic, political and social contexts in which they operate and, in particular, the trends established by our market and information-based society.[245]

The EU Digital Single Market aims to create 'a single and competitive digital market capable of promoting research and innovation based on the intensive exploitation of data sets and ensuring the protection of the rights and freedoms of individuals'.[246] Accordingly, a European Data Strategy[247] has been designed and promoted to allow data to flow freely within the EU and across sectors for the benefit of businesses, researchers and public administrations. The core idea is that data-driven research and innovation can bring major and concrete benefits to society, including personalised medicine, improved mobility, better policy-making and upgraded public services. To this end, through the European Data Act, proposed in February 2022:

> The Commission aims to make more data available for use, and set up rules on who can use and access what data for which purposes across all economic sectors in the EU. The new rules are expected to create €270 billion of additional GDP for EU Member States by 2028 by addressing the legal, economic and technical issues that lead to data being underused.[248]

The implementation of such a strategy in the field of biomedical research stakes everything on personalised medicine. Accordingly, in 2018, the European Commission's Communication on enabling the digital transformation of health and care in the Digital Single Market was adopted, identifying three main priorities: i) citizens' secure access to their own health data, including across borders; ii) personalised medicine through a shared European data infrastructure; iii) citizen empowerment with digital tools for user feedback and person-centred care.

On the basis of this premise, I now critically analyse and discuss a negative consequence of this economic and political commitment in the field of biomedical research – the trend

[245] I. de Lecuona Ramírez, 'La tendencia a la mercantilisación de partes del cuerpo humano y de la intimidad en investigación con muestras biológicas y datos (pequeños y masivos)'. Chapter 10 in Maria Casado (ed.) *De la solidaridad al mercado: el cuerpo humano y el comercio biotecnológico* (Edicions de la Universitat de Barcelona 2017) 267-295.; R. García Manrique (ed.) *El cuerpo diseminado. Estatuto, uso y disposición de los biomateriales humanos* (Aranzadi, Cizur Menor 2018)
[246] https://eufordigital.eu/discover-eu/eu-digital-single-market/ Accessed 21 March 2022.
[247]https://ec.europa.eu/info/strategy/priorities-2019-2024/europe-fit-digital-age/european-data-strategy Accessed 21 March 2022
[248] https://ec.europa.eu/commission/presscorner/detail/en/ip_22_1113 Accessed 21 March 2022

towards the commodification of biospecimens and datasets – and I maintain that this tendency represents a threat to the ethical foundation of human-subject research based on altruism and the principle of non-commercialisation of the human body.

As argued by Casado, the national and international ethical and legal framework of biomedical research:

> Places the transactions that concern the human body and its parts under a framework of no profit and solidarity. In principle, it can be said that, invoking human dignity, only things can have a price and, therefore, the human body and its components are outside the market. But this point of departure, which is generally accepted, comes into open conflict with the reality of the practices carried out in the field of health and research. […] To such an extent that, even at the theoretical level, analyses are being carried out that reformulate the established to accept profit also in this field. [249]

The Council of Europe's Convention on Human Rights and Biomedicine (the Oviedo Convention)[250] represents a cornerstone for research ethics because it is the only international legally binding instrument on the protection of human rights in the biomedical field. Its Article 2 establishes the primacy of the human being, indicating that the interests and welfare of the individual should prevail over those of society or science. Accordingly, Article 21 prohibits financial gain: as such, the human body and its parts should not be used for profit.

Similarly, the EU Recommendation Rec(2006)4 of the Committee of Ministers, to Member States on research using biological materials of human origin, establishes in Article 7 a prohibition of financial gain: biological materials should not, therefore, be used for financial gain.[251] In other words, the fundamental idea underlying biomedical research ethics is that the human body has a special dignity that should prevent the market from putting a price on it and commodifying it.

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[249] M. Casado '¿Gratuidad o precio?: Sobre el cuerpo humano como recurso'. Chapter 1 in *M. Casado, (ed.) De la solidaridad al mercado: el cuerpo humano y el comercio biotecnológico (*Edicions de la Universitat de Barcelona 2017) 18. [My translation]

[250] Council of Europe, 'European Convention on Human Rights and Biomedicine' April 4, 1997, ETS. no 164, Available at https://www.coe.int/en/web/conventions/full-list?module=treaty-detail&treatynum=164

[251] Recommendation Rec(2006)4 of the Committee of Ministers to member states on research on biological materials of human origin and its Explanatory Memorandum

These considerations also apply in principle to biobanks as collections of human biological samples and associated personal data. In this regard, a valuable example of national regulation of biomedical research and biobanks is represented by the Spanish *Ley 14/2007 de Investigación Biomédica* (LIB). In my paper *Regulating Biobanks: An ethical analysis of the Spanish law and the new challenges of the big data-driven biomedical research,* I explained that:

> In this regulation, free donation of human organs and tissues is a well-established ethical principle and is considered contrary to the dignity of the human being to trade with elements of the body. In particular, what stands out is the strong reference to the principle of altruism and the emphasis on no commercialisation of the human body or its parts. In line with the Council of Europe Convention for the Protection of Human Rights,[252] in its art. 7 the LIB states that 'the donation and use of human biological samples shall be gratuitous, whatever its specific origin, and the compensation that is provided for in this Law can in no way be of lucrative or commercial nature'. In other words, the Spanish law allows biobanks to charge for obtaining, handling, shipping and distribution of samples for the sake of its own sustainability but, at the same time, it respects the principle of no commercialisation of the human body which is considered the bulwark of the protection of the human dignity.[253]

These national and international frameworks that, in principle, should protect research participants against the commodification of their bodies, parts and associated data, today clash with the actual practice of biomedical research, giving rise to the significant contradiction reported by Casado:

> How is it possible that the principles of global justice and respect for recognized human rights continue to be considered valid, and yet the commercialisation of the human body, its parts and components is increasingly accepted.*[254]*

[252] Council of Europe, *European Convention for the Protection of Human Rights and Fundamental Freedoms, as amended by Protocols Nos. 11 and 14*, 4 November 1950, ETS 5, available at: https://www.refworld.org/docid/3ae6b3b04.html [accessed 12 October 2020]
[253] S. Iacomussi, 'Regulating Biobanks: An ethical analysis of the Spanish law and the new challenges of the big data-driven biomedical research' (2021) RBD. Revista de Bioética y Derecho, 215–233. I wrote this paper while a visiting student at the Bioethics and Law Observatory at the University of Barcelona. The research that I conducted during that period and the drafting of this paper gave me a good understanding of the ethical and legal framework that regulates biomedical research and biobanks in Spain.
[254] Casado (n 51) [my translation].

The reality that we must face is that the fundamental notion of the dignity of the human body that permeates biomedical research is being challenged by the combined power of two forces. On the one hand, it is under attack from the growing trend to apply criteria that prioritise commercial relationships in fields that were traditionally immune to them. In other words, under the current framework of neoliberal globalisation, the market puts a price on and objectifies human biological samples and associated personal data, and science and biotechnology become indispensable operators of this process. On the other hand, the emergence of the digital society and the consequent datafication of health and biomedical research has created a new economically valuable asset, that of biomedical personal data, which forces us to address questions that until now were not considered to belong in a research-related context:

> How should we regard our role in relation to our own data and its contribution to the collective? Are we shareholders of an economically valuable asset, or are we joint owners or perhaps stewards of a public good or common resource? What new relationships—among people, populations, health care providers, researchers and companies—are created by the use of big data, or further, by its commercialisation?[255]

In other words, in the field of genetics research, biomedicine and biobanks, we are already witnessing a tendency towards the exploitation and monetisation of personal data that involves extracting new value from data and making a profit from it.

Based on the above, I argue that we must fight today for participant protection in biomedical research and especially biobanks, because the combined forces of the market and digital society allow human biological samples and health-related data to be traded in exchange for money in contexts that should be purely research-oriented and informed by values that are constitutionally extraneous to the language and logic of the market. In my view, human biological samples and the associated personal data collected by patients and participants in the context of a public healthcare service, hospitals and biobanks for research purposes – and thus, within an ethical and legal framework of non-commercialisation and respect for the dignity of the human body – should never be traded in exchange for money.

[255] Chan (n 33) 12.

3.1. The cases of 23andMe and VISC+/PADRIS

To support my argument, the following cases may help to explain what is ethically questionable in the phenomenon that I have just described and why we should fight it.

The first case concerns the tendency to accumulate personal information and monetise it through 'direct to consumer (DTC) genetic testing'; the second regards the exploitation and the commercialisation of public health datasets.

The aims of the following critical analysis are, firstly, to show the pervasiveness of the trend toward the commodification of human biological samples and personal data collected for research purposes that occurs in both private and public sectors in biomedical research and often sees the two in partnership. Secondly, it aims to show the risks we run if we allow this to become the future direction of data-driven biomedical research: how we – as a society – may be affected by companies or corporations accumulating our health-related information and making money from this process. It can be turned into an instrument of power in the hands of third parties that may be used against us, for example, by creating health-risks profiles and selling them to private insurance companies.[256] Thirdly, this analysis aims to highlight that these cases present ethical issues that require moral assessment to be extended beyond legal compliance and consent procedures.

23andMe

The first case concerns the tendency to accumulate personal information and monetise it through 'direct to consumer (DTC) genetic testing', using genetic home-testing kits sold directly to consumers by private companies to provide insights about their genetic information (ancestry, health traits and health risks) from a saliva sample. Unlike clinical-based genetic tests which are ordered, interpreted and disclosed by a physician or other healthcare professional, the ordering and return of results from these DTC genetic tests does not involve healthcare professional engagement and, usually, the interpretation of the results is left to the customer.[257]

[256] M. R. Llàcer, M. Casado & L. Buisan, *Document sobre bioètica i Big Data de salut: explotació i comercialització de les dades dels usuaris de la sanitat pública* (Edicions Universitat Barcelona 2015).
[257] The practical limitations and ethical issues of such enterprises have been discussed in the scientific literature. See, for reference: S. Hogarth, G. Javitt & D. Melzer 'The current landscape for direct-to-consumer genetic testing: legal, ethical, and policy issues' (2008) Annu. Rev. Genomics Hum. Genet., *9*, 161–182;

23andMe is a well-known DTC genetic-testing private company in the USA, which sells genetic tests online offering various services in return.[258] In particular, it promises to explore three areas from the sequencing of customers' DNA: i) health predispositions: the test can provide information on the likelihood of the customer developing certain health conditions based on their DNA; ii) ancestry composition: the test allows the customer to discover where in the world their DNA is 'distributed' and, in turn, potentially to connect with relatives comparable with ancestries and traits; iii) traits features: the test shows the customer how DNA can influence physical features (e.g. hair photobleaching, freckles). Overall, the appeal of these services lies in knowing that such information can help customers to take action on their health and well-being.

After signing up to 23andMe via the company's website and placing an order, all customers need to accept the company's Terms of Service, which set out the contractual basis for the genome sequencing services offered. At this point, a second level of customer involvement should be considered. Customers can opt into 23andMe's research activities and agree to their samples and associated personal data being retained for biobanking.

For both options – 23andMe's testing service and research – personal data are said to be encrypted (not anonymised), protected and under the consumers' control.

Customers who opt into 23andMe's research sign a research consent that 'allows 23andMe researchers to use certain information (including your Genetic Information and your responses to research surveys) to study a wide variety of research topics' and are told that 'taking part in this research is completely voluntary, and you can change your consent choice at any time without affecting your access to the 23andMe product or services'.[259]

Regarding collaboration with third parties, the research consent states that some 23andMe research is conducted in collaboration with third parties, such as non-profit organisations, pharmaceutical companies, or academic institutions and that they 'may share summaries of research results, which do not identify any particular individual**,** with qualified research collaborators and in scientific publications'.[260]

T Caulfield & A. L McGuire, 'Direct-to-consumer genetic testing: perceptions, problems, and policy responses' (2012) Annual Review of Medicine, *63*, 23–33.

[258] https://www.23andme.com/?evr=epv

[259] https://www.23andme.com/about/consent/

[260] ibid.

For the purposes of my ethical case analysis, I focus on how the company uses customers' samples and associated data for research, with the aim of showing the relevance of the ethical issues at stake. In the first place, it is important to note that the informed consent signed by customers for their samples and data to be used for 23andMe's research is based on an opt-in model and, in the case of collaboration with third parties, is reduced to an eventual disclosure *ex-post*, which is different from a previous and specific consent.[261]

In the second place, it is important to acknowledge, following Stoekle and colleagues' argument, that it may be the case that from the outset the primary objective of 23andMe was two-fold:

> Promoting itself within the market for predictive testing for human genetic diseases and ancestry at a low cost to consumers, and establishing a high-value database/biobank for research (one of the largest biobanks of human deoxyribonucleic acid (DNA) and personal information).[262]

Accordingly, 23andMe have two different kinds of customers: i) people who seek insights into their genetic make-up for a number of different reasons; and ii) third parties such as pharmaceutical companies who want access to the large datasets of genetic, phenotypic, lifestyle-related and other self-reported information that the company collects from customer data and then sells access to.[263]

On the basis of these considerations, I will now explore what is ethically questionable about the behaviour of 23andMe, which was chosen as a high-profile example of several DTC practices that raise ethical, legal and social issues.[264]

I argue that 23andMes' research activities raise three problematic points:

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[261] M. Allyse, '23 and Me, We and You: direct-to-consumer genetics, intellectual property and informed consent' (2013) Trends in Biotechnology, *31*(2), 68.
[262] H. C. Stoeklé and others, '23andMe: a new two-sided data-banking market model' (2016) BMC Medical Ethics, *17*(1), 1–11.
[263] A. E. Raz and others, 'Transparency, consent and trust in the use of customers' data by an online genetic testing company: an Exploratory survey among 23andMe users' (2020) New Genetics and Society, *39*(4), 459–482.
[264] S. L. Tobin and others, 'Customers or research participants? Guidance for research practices in commercialisation of personal genomics' (2012). Genetics in Medicine, *14*(10), 833–835.

- The company accumulates datasets of personal data for their commercial value. The information asked of customers goes beyond the genetic information extracted from DNA sequencing, including, for example, follow-on surveys about health and lifestyle.

- The company makes financial agreements (see below for the best-known case) to transfer the accumulated datasets to third parties that use them for research purposes.

- Even if the possibility that customers' data will be shared is contemplated by the research consent signed by them, the transfer takes place without their explicit consent.

Therefore, what is ethically questionable here is 'the extent to which the company assures – or should be required to assure – that its customers are aware of how exactly their data is being used'.[265] Even if the possibility of making customers' data available to third parties is contemplated in the original agreement between the customer and the company, there is an ethical assessment of this practice that goes beyond legal compliance – in this case, compliance with the conditions stated in the consent form signed by the customer.

This appears clear in the following facts. In 2018, 23andMe announced a collaboration with GlaxoSmithKline (GSK) to use its encrypted aggregated datasets to develop pharmaceutical drugs and thus attracted a $300 million investment from the pharmaceutical giant.[266] By that time, 23andMe had collected personal data from over 8 million customers, accumulating a treasure trove of genetic data that represents by far the largest collection of gene-linked health data anywhere in the world. The goal of this collaboration was to combine 23andMe's genetic databases with GSK's scientific knowledge and commercialisation expertise to drive disease progression research, discover novel drug targets and develop new therapies.[267]

Read against the previous ethical considerations, it should now be clear why there is still something morally problematic about this transition, although the goals of the collaboration are worthy and aimed at the common good and shared benefit.

[265] A. E. Raz and others (n 66).
[266] https://www.nytimes.com/2021/09/20/opinion/23andme-dna.html?
[267] https://www.gsk.com/en-gb/media/press-releases/gsk-and-23andme-sign-agreement-to-leverage-genetic-insights-for-the-development-of-novel-medicines/

I believe that the core of the ethical conflict lies at the level of trust – or rather, the breach of trust. Indeed, it is difficult to imagine that 23andMe's customers, who once absently ticked a box consenting to the use of their data, do not feel that they have been exploited with their data sold to enrich the pockets of a commercial enterprise.[268] As mentioned above, the question of meaningful and valid consent remains relevant even if potential collaboration with third parties was contemplated in the original agreement and the operations are legally compliant. The question to be addressed is whether or not it is ethical that 'people are asked to agree to something that they are unlikely to have read, and that […] may not have expected'.[269] The answer is that not all customers may have been aware of the possibility of such a commercial partnership when they signed up. Thus, it can be argued that 23andMe – as well as other private companies – is an expression of digital society's tendency towards the exploitation of personal data in research contexts without the knowledge of research participants.

VISC+/PADRIS Project

The second case analysis focuses on the Catalan government's programme – established in 2013 and formerly known as VISC+, but now called PADRIS – on data analysis in health research. It has been chosen as an example of political commitment towards the intensive exploitation of health-related datasets and allows me to exemplify the ethical challenges raised by the digital society in the field of biomedical research.

The Catalan VISC+ project (the acronym stands for 'Adding Value to Health Information in Catalonia') was promoted by the Catalan Agency for Health Information, Assessment and Quality (AQuAS) of the Generalitat of Catalonia and advertised as follows:

> The Catalan health system takes care of 45 million patients annually, prescribes 140 million electronic prescriptions and has 60 million documents in its shared medical record. All of these data can be very important for the scientific community in order to progress in medical research. The VISC+ Project, the differential value of which lies in the reuse of data, represents the arrival of Big Data in the health world. This project can help to improve treatments and to develop the research field.[270]

[268] https://www.bloomberg.com/news/features/2021-11-04/23andme-to-use-dna-tests-to-make-cancer-drugs
[269] A. E. Raz and others (n 66).
[270] https://ticsalutsocial.cat/noticia/the-bioethics-committee-of-catalonia-approves-the-visc-project/

The explicit objective – according to its promoters – was to make citizens' health information available to healthcare personnel, health-related businesses and biomedical researchers in order to improve health care services and research and 'add value' to knowledge'.[271] The project was based on the use of personal data from various existing databases in the Catalan health care system – in particular SIDIAP (Information system for the development of research in primary care) and HC3 (Shared clinical history of Catalunia)[272] – in which data on the clinical histories of health care system users were collected together with other relevant information regarding the social and health situations of each individual, on a presumed consent and opt-out basis. Clearly, this involves extremely sensitive personal information that, in the case of HC3, was collected with explicit objectives and handled within specific parameters of confidentiality and security.

Despite its legal compliance with national privacy regulations and the fact that it was designed as a tool to offer benefits for the health care system and the population, the VISC+ project – based on the re-use of personal data accumulated under a previous framework (HC3) – raised significant ethical issues to the point where the Catalan Parliament and the Bioethics and Law Observatory of the University of Barcelona argued against its implementation.[273] The core of the ethical conflict at the time was, as argued by de Lecuona and Villalobos-Quesada, the fact that VISC+, based on opt-out presumed consent:

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[271] M. R. Llàcer and others, *Document on Bioethics and Big Data: Exploitation and Commercialisation of User Data in Public Health Care. Bioethics and Law Observatory*. (University of Barcelona 2015).

[272] Llàcer (n 74) 58. Llàcer notes, in particular, that the HC3 'collects data on health care system users' clinical histories and pharmaceutical consumption as well as other relevant information regarding the identification and social and health situation of each individual in the public system. The HC3 also contains information on test results and diagnoses that includes metabolic and biochemical data, as well as genetic diagnostic data to identify carriers of hereditary diseases or to determine risk or susceptibility to complex diseases. These databases contain 'user files', under the responsibility of the Health Department of the Generalitat of Catalonia […]. The explicit objectives of the HC3 are: a) to improve the health care assistance provided to the population through a tool that facilitates the work of health care professionals, and b) to provide a new health care model by permitting health care centres in the public health care network access to available relevant information on their patients in a quick, secure and confidential manner'.

[273] The Observatory published a Declaration on Bioethics and Big Data that addressed the implications of the exploitation and commercialisation of user data in the public health care system, with the goal of guiding policy-makers. The Declaration was followed by the Catalan Parliament, which urged that the project be stopped and, instead, a public program developed that would not allow the commodification of personal healthcare data.

I de Lecuona & M. Villalobos-Quesada, 'European perspectives on big data applied to health: The case of biobanks and human databases' (2018) Developing world bioethics, *18*(3), 291–298, 294.

The new project (PADRIS – Public Data Analysis for Health Research and Innovation Program) was implemented in 2016. It offers restricted data access to public and certified researcher and health- related institutions and has an obligation to inform citizens about the model of informed consent chosen, the opt-out options, who may have access to their personal information and to which possible ends it may be used.

> had the goal of offering a unified Catalan health database to third parties for health-related research, opening the door to those seeking economic gain. This objective is in direct conflict with the principle of 'purpose limitation' recommended by the European Commission, which considers explicit consent necessary when personal data is used for commercial purposes.[274]

The Declaration on Bioethics and Big Data issued by the Bioethics and Law Observatory with the goal of guiding policy-making – made in response to the need to address the implications of the exploitation and commercialisation of user data from the public health care system within the VISC+ Project – identified two main areas that contribute to making the project ethically questionable.

The first is the possible violation of citizens' rights. In today's digital society, the right to privacy and confidentiality are endangered by the technical potential to re-identify personal data and any claim of anonymisation of personal data cannot be considered a guarantee of protection. Any health-related projects should ensure the implementation of adequate mechanisms of data protection, but these were not considered by VISC+ project.

The second regards the lack of transparency and informed debate on how health-related data are used. In particular:

> When the HC3 was established, individuals did not receive sufficient information about this massive data collection, nor were they advised at any time that this data could be re-used for other purposes, including commercial ones. Nor was it considered that the transfer of data acquired from users of the public health care system for other purposes than health care was the 'price' for free assistance[275].

Thus, the problematic element from an ethical point of view was the fact that the data collected by HC3 with the presumed consent of the data subjects (the opt-out model) were intended to be re-used in the VISC+ project without – despite what would be expected under the principle of 'purpose limitation' – any guarantee on the limitation of these secondary uses to scientific use (epidemiological, research and teaching) and the improvement of the public health service. Moreover, no guarantees were considered to avoid unwanted use of

[274] Ibidem.
[275] Ibidem.

personal data, or commercial use by businesses in the health care sector (health insurance firms, pharmaceutical companies, financial and other entities).

To conclude, the two cases presented above offer some lessons for the relevance of the ethical issues at stake for biomedical research in a data-driven society and economy. First, the case of 23andMe shows that it is extremely easy today to lure customers in with the promise of answers about their genetics and health, then quickly move to monetise that information. This case gives a valuable insight into the importance of ethical assessment of practice beyond informed consent, because it is there that the core of the ethical conflict lies: is it ethically acceptable to make financial agreements to transfer genetic and health-related personal data to third parties without having previously ensured that the data-subjects were completely aware of how precisely how their data would be used in the future?

Secondly, the case of VISC+ demonstrates that our systems rely on the exploitation of personal data including in biomedical research and health care contexts, often based on opt-out or presumed consent. The lesson here is the importance of fostering transparent governance mechanisms in such projects – even those conducted by public institutions – to include public engagement in promoting informed dialogue with society and an ethical assessment of practice from roots up to ensure compliance with the ethical standards.

3.2. The case of disguised market of biobank resources

This section will now clarify how the phenomenon of commodification of biospecimens and datasets affects biobanks and their governance. It will address the heart of my argument and analyse the challenges facing biobank governance in a digital society. As suggested by de Lecuona, 'from a mercantilist point of view, biobanks are gold mines to be exploited'.[276] Given the trend towards the exploitation and commercialisation of human biological samples and personal datasets in the context of biomedical research, it is of fundamental importance that those who manage biobanks and are involved in them – including biobank external ethics committees – share the same values and have sufficient scientific, technical and ethical expertise to avoid chasing profit at the expense of research priorities and values. Firstly, I believe that it is useful to explain what we mean by the commercialisation and

[276] I. De Lecuona Ramírez (n 47).

commodification of human biological samples and associated data in the field of biobanks. Evers and colleagues have explained:

> In the context of biobank research there are two distinct aspects of commercialisation to consider, based on whether biological samples give rise to financial gain indirectly or directly. In the first case, samples are used for research to gain knowledge that is then sold. In the second case, access to samples, or even the samples themselves, are bought and sold.[277]

The fact that biobanks have associated commercial interests should not surprise us. Indeed, biobanks face a sustainability problem in terms of their long-term maintenance since high-quality biobanking facilities are costly; there is, therefore, a need to attract public and/or private funding.[278] Furthermore, it goes without saying that the process involved in translating discoveries into new innovations always requires financial investment and the interests involved in such transition may affect biobank governance.[279]

In response, there is the possibility to leverage directly the economic value of the biobank's samples and data, transforming them – or access to them – into tradable commodities.[280] As anticipated in the previous paragraphs, I argue that here lies the ethical problem, namely in situations in which samples and data collected for research purposes become commodities to be traded in exchange for money with third parties.

The case of the Italian Telethon Network of Genetic Biobanks (TNGB) provides a concrete example of the risks of the commodification of samples and personal data in the context of biobanks, and offers a context against which the relevance of the ethical issues behind this tendency may be discussed.

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[277] K. Evers, J. Forsberg & M. Hansson (n 44).
[278] A. Turner, C. Dallaire-Fortier & M. J. Murtagh, 'Biobank economics and the "Commercialisation Problem"' (2013). Spontaneous Generations: A journal for the history and philosophy of Science, *7*(1), 69-80.
[279] H. Yu, 'Redefining responsible research and innovation for the advancement of biobanking and biomedical research' (2016). Journal of Law and the Biosciences, *3*(3), 611–635.

[280] M Maseme, 'Commodification of biomaterials and data when funding is contingent to transfer in biobank research' (20219 *Medicine, Health Care and Philosophy* 24(4), 667-675.
In simple terms, commodifying things amounts to a sale. In the context of this paper, the commodification of biomaterials and data (interchangeably referred to as materials herein) refers to the extent to which materials become commodities of trade and are transferred for money.

The case refers to a recent study[281] – to which I have contributed as co-author - conducted within the TNGB focusing on the governance of access to samples and data to highlight the strategies employed by the TNGB to manage access to its collection. The paper discusses the main issues faced by the Access Committee – the ethical oversight body appointed to evaluate access requests from external researchers – to stress the ethical principles underlying TNGB's access policy. In reviewing the history of the assessment process for access requests, we found that the use of private intermediaries to access the biobank's resources in exchange for money has repeatedly been considered a sufficient reason to refuse the request for access. Specifically, the results show that, in the last 10 years, the Access Committee rejected many requests made by individuals working for private companies which approached TNGB's biobanks with requests for huge numbers of samples (despite the rarity and scarcity of the samples since we are talking about rare diseases biobanks) and with a poor description of the research projects for which they intended to use the requested samples. In addition, the Access Committee was concerned about the lack of clarity over the final recipients of the samples. Accordingly, the Access Committee's reason for rejecting such requests was stated to be that controversial commercial interests had been perceived that conflicted with their mission, which focuses on the common benefits of scientific investigation and public health; for this reason, samples and data are made available to researchers for biomedical research purposes only.

I believe that the TNGB case represents an outstanding example of good governance, in the sense that both the operation manager and the Access/Ethical Committees were aware of the risk of commodification and were ready to combat this trend toward profiting from samples and data. As argued by de Lecuona:

> Research resources and infrastructures such as public biobanks should not be associated, for example, with what are known as intermediaries of biological samples of human origin; that is, companies whose job it is, among other services, to position the samples in return for money. These companies demand, moreover, the commercial exclusive for 'placing' samples for financial gain that have been donated by citizens altruistically, free of charge.[282]

[281] S. Iacomussi and others, 'Governance of Access in Biobanking: The Case of Telethon Network of Genetic Biobanks' (2021) Biopreservation and Biobanking, *19*(6), 483–492.

[282] I. de Lecuona Ramírez (n 47).

Given that sharing biobank resources entails the concrete risk of the misuse of samples and data collected by a biobank, conflicts with its mission and a breach of trust with research participants, it is fundamental that each biobank implements actions:

> … to guarantee that samples and data [ ] available to researchers for biomedical research purposes are based only on the respect of the principle of gratuity of the human body, which is consistent with an understanding of biobanking as a system based on altruism and solidarity and, at the same time, on the promotion of individual responsibility of each researcher [when dealing with biobanks' resources].[283]

It is worth at this point engaging in critical reflection – as with the above case analyses – on what is ethically questionable in the use of private intermediary companies to approach biobanks and trade biobank samples and data with third parties in exchange for money. I argue that the problematic element lies in breaking into a genetic and health-related data market in the disguise of research in the biobanking field. The ethically controversial consequences of such inappropriate practice are at least twofold. First, the morally problematic exploitation of materials and data donated within a solidarity-based framework introduces tensions to the values and mission of biobanks by threatening to undermine both the notion of altruistic donation and the notion that biobanks serve the scientific and public good.[284]

Secondly, such practice brings inevitable harms and difficulties regarding biobank participants' control over how their samples and data are used and with whom they are shared. I refer here to the fact that commodification raises ethical, legal and social issues around consent, intellectual property and ownership. As argued by Turner and colleagues, it may be the case that:

> Participants may not want their samples to be used for commercial research; the patenting of genes may lead to expensive therapies and diagnostic tests, which undermine the equity of biobank's benefits; or that fear of litigation may stifle innovation.[285]

[283] S. Iacomussi and others (n 83) 8.
[284] A. Turner, C. Dallaire-Fortier & M. J. Murtagh (n 80).
[285] ibid.

The relevance of the ethical issues at stake is to be found in the potential for inappropriate practices in biobanking generated by the intrusion of a data-driven market in the guise of research. Such a tendency is problematic – and hard to recognise for anyone not trained in detecting bioethical issues – because it clashes with the purpose of sharing biobank samples and data that is, as established by national and international laws, to share knowledge with the scientific community rather than to obtain profit from it. Furthermore, it generates a problem of trustworthiness: it wrongs patients and society for a biobank to disguise the economic exchange of human biological samples as a research project.

In conclusion, the case of private intermediary companies seeking access to biobank resources shows that a conceptualisation of appropriate biobank governance in the digital age should prioritise as follows:

> The impact that in the context of research these practices have on people's rights calls for a change in the dynamics of who is researching, who is directing, who is assessing and controlling and who is authorizing the research. This also leads to a demand for changes in the market and to consider as a point of departure that bodies and body parts (samples included), as well as personal health data, should be kept out of commerce, and they should of course not be quoted on the stock exchange. Compliance with this condition seems impossible in the market society in which we live, where even university professors are obliged to place their knowledge and innovation on the market.[286]

4. Biobanks, market and data: filling conceptual gaps

Given the challenges for biobank governance that I have described in this chapter – namely the risks brought by the digital age that endanger the privacy of biobank participants, and the tendency towards a commodification of biobank resources in line with the data-driven economy pursued by the European Union – I claim that there is a need to probe more deeply through a bioethical inquiry before moving to the conceptualisation of an appropriate governance for biobanks in data-driven biomedical research in the next chapter.

[286] I. de Lecuona Ramírez (no 47).

The first issue regards the relationship between biobanks and the market, to strengthen my arguments against the commodification of biobank resources by explaining how the intrusion of market logic and values has the potential ethically to corrupt biobanking practices. The second concerns, rather, the relationship between biobanks and data, to emphasise the need for ethical and legal guidance with an updated understanding of biobanks, moving from a sample-centric to a data-centric approach to better tackle the challenges brought by the digital paradigm.

Biobanks and the market

I have described above the ethical issues implied by the tendency towards the commodification of biobank resources. Biobanks are subject to the rules of capitalism and to a market that now sees data as the new fuel. In particular, health-related data is the new frontier of business and, from an ethical perspective, it is important to reflect on how to take advantage of this as a society and not leave it to the bigger platforms.[287]

In this section, I reflect on why the intrusion of market values and priorities could be considered ethically wrong in the context of biomedical research and, in particular, biobanks. I rely on Sandel's well-known essay 'What money can't buy' and his analysis of the moral limits of a neoliberal and globalised market approach that has, in recent years, expanded its norms and values into spheres of life normally governed by non-market logic, such as healthcare, education, reproduction and social practices.[288] From this phenomenon, he derives the definition of a market society as a way of living in which market priorities and values permeate every human activity.

The core of Sandel's critique of the market society is based on two main arguments: first, he maintains that the widespread tendency toward commodification (i.e. putting a price on everything) may promote the wrong way to evaluate the good and, consequently, its corruption. Secondly, he argues that the values embodied by market logic may crowd out non-market norms and values.

[287] S. Zuboff, *The age of surveillance capitalism: The fight for a human future at the new frontier of power: Barack Obama's books of 2019* (Profile books 2019). M. Mazzucato, *The value of everything: Making and taking in the global economy* (Hachette UK 2018).

[288] M. J. Sandel, 'What money can't buy: the moral limits of markets' (2000) Tanner Lectures on Human Values, *21*, 87–122.

Applying this critique to the field of biobanks, I argue first that the fact that biobanks are imbued by the market approach and influenced by it negatively affects the meaning and perception of biological samples and related data stored in it and the understanding of biobanking practice itself. Secondly, I argue that the invasion of market trends in the biobank field risk crowding out core values and priorities on which biobanks have been built (e.g. non-commercial and research purposes).

The heart of the issue lies in the trend toward the commodification of biobank samples and health personal data, and their treatment as goods traded on a research market based on their potential for therapeutic products and scientific patents.

How we value human biological samples and associated health personal data is closely related to our ethical and legal conception of the human body. The literature on this topic is extensive, encompassing many interpretations, mostly dependent on the philosophical and juridical traditions of the different scholars and countries. Indeed, despite a general agreement on the view of the human body as an entity worthy of special dignity, it is much harder to reach a common understanding of its separate components and parts. Accordingly, regulatory frameworks on the use of human biological materials take different forms depending on the conception they want to defend. In this regard, Tallacchini makes an interesting distinction:

> In response to the various questions that have arisen around the biobanking of human biological materials and information, two strategies have been adopted in the US and in Europe; these are distinguished by their respective focus on two main legal concepts: individual property rights and individual autonomy—or the right to privacy.[289]

Specifically, the European ethical and legal tradition has framed the regulation of human biological samples within the concepts of autonomy, dignity and the right to privacy, leading to the prohibition of gaining profit from the body and its parts.[290] In contrast, the US normative framework has primarily defined the question of human parts in terms of property. As such, the regulation seems more permissive when it comes to the trading of human biological

[289] M. Tallacchini, 'A participatory space beyond the "autonomy versus property" dichotomy', in *Ethics, Law and Governance of Biobanking* pp. 21-38 (Springer 2015) 21.
[290] Cfr. Directive 2004/23/CE; Regulation 1394/2007/CE; Recommendation 4(2006)

materials, prioritising the need not to damage research assets and pharmaceutical corporations.

Since this dissertation takes as a reference the European bioethical and juridical conception of the body and its parts, the critique of the commodification of human biological samples stored in biobanks could be articulated as follows. Firstly, applying a market approach to the collection and sharing of biosamples and related data may promote a degrading vision of the human body, threatening its dignity. Secondly, putting a price on biobank resources significantly undermines the values of both altruism and solidarity that underpin their collection and the mission of biobanking itself – to promote the sharing of materials and data between the scientific community to foster biomedical research.

To sum up, the application of Sandel's corruption argument to the context of biobanks presents a strong objection to the commodification of human biological samples stored in biobanks because it corrupts the meaning and the value of those resources as well as the fundamental purpose of biobanking.

My second argument is based on the assumption that the commodification of biobank samples and data promotes an unhelpful attitude towards biobanks. Indeed, in continuing his analysis of the moral limits of the markets, Sandel observes that the introduction of a market approach in areas constitutionally untouched by this logic displaces their norms, fostering negative attitudes towards the goods and practices. In the specific case of biobanks, two negative consequences can be seen in this respect. Firstly, the allocation of a market value to human biological samples and associated data could promote a negative attitude within the governance of biobanks and overturn the hierarchy of priorities. In particular, it can shift the focus from participants' rights to the interests of other stakeholders. This represents a problem, insofar as the balance among the various actors and interests involved in biobanking has been always difficult to achieve and is based on a fragile equilibrium between individuals' rights and the common good. Secondly, the commodification of a practice based on an altruism model is likely to replace its foundational norms with lower standards. For instance, we run the risk of undermining the relevance of research advances and public benefit by profit-oriented measures.

In summary, the replacement of constitutional norms – such as non-commercialisation, the common good, research orientation and best possible use – by market norms in the context

of biobanks can erode the moral commitment of the donation and a civic sense of duty as well as encouraging citizens to participate for the wrong reasons.

Biobanks and data

Following the paradigm shift in biomedical research and the new ethical imperative to protect personal data in order to protect the research participants, I argue that too little attention is still paid to the role and importance of data in biobanks. This is true at the level of both legal regulation[291] and ethical guidelines[292] which, in my opinion, reflect the common understanding of biobanks as sample-oriented. I argue that a gap exists between how scientists look at biobanks as a data mine and how the ethicists, regulators, policy-makers and the general public understand them. This represents a problem because the way in which the regulations, ethical guidance and the public perceive biobank samples and the handling of those samples is a discriminating factor in achieving an ethical governance of biobanks, especially in terms of the protection of personal sensitive information. If the biosamples collected by biobanks are seen only in terms of physical matter by law and research ethics, we will continue to have inadequate governance of biobanks.

As argued by Quinlan and colleagues, in the context of data-driven biomedical research:

> It is much more useful to think of modern biobanking as an informatics project supported by a high-quality, scientifically driven tissue collection and storage strategy, rather than as a high-quality tissue collection and storage strategy supported by an IT system. […] It is a misconception to believe a lack of samples prevents research – it is more often a lack of data that prevents research, and samples are a mechanism for generating data that is missing.[293]

Similarly, Hainaut and colleagues have recognised that the conceptual overlap between samples and data has prompted a change in how biobanking should be understood:

> With the rapid development of very high-throughput methods to extract large-scale molecular information from smaller and smaller biospecimens, biobanking should be

[291] D. Hallinan & P. D. Hert, 'Many have it wrong—samples do contain personal data: the data protection regulation as a superior framework to protect donor interests in biobanking and genomic research' in *The ethics of biomedical big data* (Springer 2016) 119-137.
[292] World Medical Association (n 35) doi:10.1001/jama.2013.281053.

[293] P. R. Quinlan and others, 'A data-centric strategy for modern biobanking' in *Biobanking in the 21st Century* (Springer 2015) 165–169.

> seen as becoming entirely interoperable with informatics and data processing, redefining the biological information contained in stored biospecimens as 'digital information in waiting'.[294]

Accordingly, one of the main challenges for biobank governance is to meet the changing requirements of biomedical research and the fact that its needs are increasingly related to creating suitable data sets; with a data-centric strategy, it is hard to envisage biobanks being able to able to meet contemporary demands.

Understanding this change is a fundamental requirement for anyone called on to regulate biobanks, to provide ethical guidelines or who is willing to participate in a biobank project. Without such understanding, we will have to continue to rely on regulations and ethical guidelines that are unable to look beyond the physical nature of samples or to adequately protect participants with regard to their data, not their bodies.

Finally, I argue that a shift from a sample-centric to a data-centric focus comes alongside crucial philosophical implications that provide important insights for our attempt to conceptualise an effective governance model. The process of datafication to which biobanks are subjected today is an expression of the prevailing digital trend in society but can also be considered a new phase in the history of biopolitics and governance that has been tracked by many scholars – from their forefather Foucault – in the evolution of modern society.[295]

According to Gottweis, biobanks contribute to the transformation of the 'old' biopolitics – and, in particular, body surveillance – to its modern version. He argues that biobanks are laboratories where the process of the decorporalisation of society reaches its peak:

> An important dimension and precondition of decorporalisation are molecularisation and informationisation. Molecular biological approaches, advances in computer and information sciences, and the convergence of these two domains have also led to a fundamental reconceptualisation of health and disease in medical discourse.[296]

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[294] P. Hainaut and others, *Biobanking of Human Biospecimens* (Springer International Publishing 2021).

[295] G. Agamben, *Homo Sacer: Sovereign Power and Bare Life* (Stanford University Press 1998); M. Foucault, *Discipline and Punish: The Birth of the Prison* (Allen Lane 1977); M. Foucault, *The History of Sexuality, Vol. 1: An Introduction* (Allen Lane 1979).

[296] H. Gottweis, 'Biobanks in action: new strategies in the governance of life' in *Biobanks: governance in comparative perspective* pp. 34-50 (Routledge 2008) 26.

In other words, following Gottweis's reasoning, biobanks are sites where the molecularisation and 'informationisation' of the human body are crystallized in the form of biological infrastructures. Accordingly, as biobanks are the key tools of biomedical research, they inevitably create new trajectories of monitoring bodies, which transform bodies of data, exploit them and extract values from them in line with the trends of digital society.

In the light of this consideration, I believe that only by seeing biobanked samples as data is it possible to understand the risks involved and adequately protect research participants.

5. Conclusions

In this chapter, I have conducted a critical analysis of the state of the art of the epistemological, practical and ethical changes brought by the digital paradigm to biomedical research, and of the political, social and economic stakes that inform the direction and the goals of data-driven biomedical research. This analysis was oriented to demonstrate that the context determines the understanding and the direction of a phenomenon. In particular, in proposing an adequate model for biobank governance in the digital society, identifying and discussing the main challenges for biobanks in their role as key infrastructures for data-driven biomedical research has been a fundamental step in reaching the goal of this dissertation.

In the first part of the chapter, I described the scope of biomedical research's paradigm shift from different points of view: the epistemological turn from knowledge-based to data-based science, how data-driven research works in practice and the critical ethical challenges. I then presented a comparison between the traditional framework for research ethics and the new features of the context in which research is conducted today. I have highlighted the fundamental incompatibility between the ethical guidance available and the challenges brought by data-driven biomedical research as regards privacy and data protection, informed consent and ethical oversight. At the same time, however, I have acknowledged that precisely because the features of data-driven biomedical research disrupt traditional ethical categories, we face a unique opportunity to update the research ethical framework.

Moving to the specific implications for biobank governance, I have argued that the research ethics framework is insufficient to protect biobank participants from the risks associated with data-driven biomedical research. In particular, the main limits were identified in the narrow conception of research governance focused on informed consent and the protection of the individual from physical rather than informational harms, the intrinsic impossibility of obtaining specific consent in biobanks and the lack of protection against risks associated with the health-related data marketplace.

The second part of the chapter focused on the ethical analysis of a fundamental feature of the contemporary context in which biobanks operate – the tendency towards the commodification of human biological samples and associated data, reflecting the prevailing

trend in the digital age towards the exploitation and monetisation of personal data. The case analyses that I conducted helped me to argue, firstly, that it is not ethically acceptable for health-related personal and sensitive data collected for research purposes to be transferred to third parties in exchange for money without having previously ensured that research participants were aware of precisely how their information would be used. Secondly, I argued that, to avoid such unethical practices in the context of private and public biomedical research, it is necessary to implement transparent governance mechanisms to foster public engagement and informed public dialogue to ensure that research participants are aware of the risks associated with participation. Finally, the analysis of a case in which private intermediary companies were used to seek access to biobank resources through requests disguised as research projects allowed me to demonstrate that this tendency has also reached biobanks and, in turn, to understand the priorities for biobank governance in the digital society.

In conclusion, I claim that a conceptualisation of an effective model of governance for biobanks in the context of data-driven biomedical research should be driven by two priorities. First, the ethical framework informing biobank governance needs to be adapted to compensate for the need for specific consent but, above all, to protect biobank participants from risks related to the secondary use of samples and personal data, such as unwanted uses, commercial uses and covert discrimination; the risks associated with technological advances such as the possibility of re-identification of encrypted data and the consequent danger for privacy; and the risks associated with the personal data marketplace, that is, the possibility that health-related data collected for research purposes may be sold to third parties without participants' knowledge.

Secondly, biobank governance must promote a way to conduct biomedical research that responds to the needs of data-driven biomedical research but, at the same time, is committed to recognising the altruistic act behind biobank participation and the values of solidarity, benefit sharing and common good that constitutionally underpin the mission of public biobanks in order to not succumb to the trend of the commodification of biobank samples and data.

Chapter 3
A societal and participatory model of biobank governance for the digital society

1. Introduction

Data-driven biomedical research has brought transformative developments in terms of the challenges and new risks associated with the participation of patients and healthy volunteers – and the use of their biological samples and associated personal data – that in the field of biobanking have serious ethical, legal and social consequences, in particular regarding privacy, informed consent and secondary uses.

A successful biobank model of governance in our digital society is one that, in response to the challenges brought by the digital paradigm for the collection, use and sharing of human biological samples and personal data, is able to empower participants and society, ensuring adequate protection for participants and the implementation of appropriate ethical procedures while providing high-quality resources to support biomedical research and innovation.

Accordingly, the first part of this chapter is devoted to a conceptual analysis of the phenomenon biobanking, aimed to identify the vision that we want to inform biobank governance and the most appropriate model to align ethical procedures with societal interests. To move to a societal and participatory model of biobank governance in a data-driven society, I propose a four-level framework, ranging from the most concrete level – the literal definition of a biobank – to the most abstract, where the ethical principles emerge. In this respect, only a broad vision of biobank that embraces all the four levels, will be able to unlock the various sticking points and tackle the ethical, legal and social issues associated with biobanking.

To progress the conceptualisation of a governance model, it is fundamental to adopt a broad vision of biobanks, focused on future directions of biomedical research and open to society, as opposed to a narrow, purely medical, vision. The second step is to shift the focus of biobank governance and research ethics from a research-sample model to a participant-data model.

In the second part of the chapter, based on this conceptual structure, I present my model of biobank governance and a proposal of the principles – transparency, data protection and participation – that I consider best suited to update current research ethics.

I explain in detail how they meet the need for an adequate ethical response to the challenges brought by the digital paradigm and how they are well-suited to enable biobank governance to achieve its goals.

2. *Pars destruens*: The deconstruction of the phenomenon

A biobank is a multifaced reality. Its complexity is reflected in the term 'biobank', which elicits a variety of assumptions and interpretations in the context of scientific literature, regulatory documents and public opinion.

To illustrate this complexity, the 'definitional issue' has been included among the ethical issues at stake in biobanking by Cambon-Thomsen and colleagues. In their pioneer analysis, having detected a wide variation in the definitions in the regulatory literature, they suggested that the question of definition is crucial because 'what is included in the definition of a biobank has ethical consequences'.[297] Accordingly, they have called for a clear definition of the term 'biobank' as a key element of implementing effective ethical management.

Following this line of reasoning, I shall attempt to clarify my understanding of the biobank in order to lay the ground for my proposed principles and governance model. With no intention to propose a definitive or unique definition, I focus rather on offering a framework as guidance to better navigate this complex phenomenon.

As recently reported by Argudo-Portal and Domènech, much effort has been made in recent decades to express the reality of a biobank in a single definition, but the risk of failing to encompass the full picture of what a biobank is and represents is never far away,[298] because, as often is the case, the 'mere' descriptive level fails to grasp comprehensively the extent of a phenomenon. Therefore, I would like, in my proposal, to go beyond the

[297] A. Cambon-Thomsen, E. Rial-Sebbag & B. M. Knoppers, 'Trends in ethical and legal frameworks for the use of human biobanks' (2007) European Respiratory Journal, *30*(2), 373–382. p. 375.

[298] V. Argudo-Portal & M. Domènech, 'The reconfiguration of biobanks in Europe under the BBMRI-ERIC framework: towards global sharing nodes?' (2020) Life Sciences, Society and Policy, *16*(1), 1–15.

‘definitional issue’ and open the way to a deeper understanding of the concept of the biobank.

As seen in the previous chapter, several challenges arise when discussing biobank governance in the digital society. Accordingly, in the following framework, I propose to look at the question differently, moving from a narrow – just medically oriented - to a broad and societal oriented vision of biobanks.

2.1. Four ways to understand a biobank

a. The biobank as a collection of human biological samples and associated data

In the last twenty years, the concept of biobank has made its way into the scientific community, and brought with it the need to define the concept and regulate its function on a scientific, social and political level. I have selected five references from legal and ethical documents, reports and guidelines released by various European leading institutions and organisations that, from the beginning of the 2000s, have shown a specific interest in regulating the field of biobanking. I am interested in examining how they have approached the concept of the biobank.

My selection was designed to provide a diversity of references, ranging from the specific field of biobanking to a global policy forum, legal documents and ethical reference texts to obtain a broad picture of how the concept of the biobank is approached in different domains.

The International Society for Biological and Environmental Repositories (ISBER), in the first edition of its report on Best Practices for Repositories in 2005, understood ‘biobank’ as a synonym for ‘repository’: ‘an entity that receives, stores, processes and/or distributes specimens, as needed. It encompasses the physical location as well as the full range of activities associated with its operation’.[299]

[299] Available at https://www.isber.org/page/BPR [Accessed 2 October 2021]. For the most recent version see for reference: L. D. Campbell and others, ‘The 2018 Revision of the ISBER Best Practices: Summary of Changes and the Editorial Team's Development Process’, Biopreservation and Biobanking 16(1): 3–6.

In 2009, the Organisation for Economic Cooperation and Development (OECD), in a report entitled 'Guidelines for Human Biobanks and Genetic Research Databases', defined biobanks as 'structured resources that can be used for genetic research and which include: (a) human biological materials and/or information generated from the analysis of the same; and (b) extensive associated information'.[300]

Moving to the legal domain, the Committee of Ministers of the Council of Europe adopted Recommendation 2006(4) which defines a populational biobank as a collection of biological materials that, among others, has the following characteristics:

> i) The collection has a population basis; ii) it is established, or has been converted, to supply biological materials or data derived therefrom for multiple future research projects; iii) it contains biological materials and associated personal data, which may include or be linked to genealogical, medical and lifestyle data and which may be regularly updated; iv) it receives and supplies materials in an organized manner.[301]

The same understanding has been endorsed by a report of the European Commission expert group on biobanks, in which they are defined as a collection of 'biological samples and associated data for medical-scientific research and diagnostic purposes and organize[d] […] in a systematic way for use by others'.[302]

This definition reflects that presented by the World Medical Association's Declaration of Taipei on Ethical Considerations regarding Health Databases and Biobanks, which approaches the phenomenon of the biobank as 'the collection, storage and use of identifiable data and biological material beyond the individual care of patients'.[303]

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[300] Available at: https://www.oecd.org/sti/emerging-tech/guidelines-for-human-biobanks-and-genetic-research-databases.htm [Accessed 29 September 2021].

[301] Recommendation Rec(2006)4 of the Committee of Ministers to member states on research on biological materials of human origin. See also Recommendation CM/Rec(2016)6: 'This Recommendation is a revision of Recommendation (2006)4 and takes into account new developments in the field of biobanking, such as the increasingly diverse origin of biological materials stored in collections, the difficulty to guarantee non-identifiability of such samples, the increasing amount of research involving materials coming from different collections, and the importance of research on biomaterials removed from persons not able to consent.' Available at https://www.coe.int/en/web/bioethics/biobanks [Accessed 5 October 2021].

[302] European Commission, Directorate-General for Research and Innovation, *Biobanks for Europe: a challenge for governance* (Publications Office 2012) 8. Available at: https://data.europa.eu/doi/10.2777/68942 [Accessed 5 October 2021].

[303] Available at: https://www.wma.net/policies-post/wma-declaration-of-taipei-on-ethical-considerations-regarding-health-databases-and-biobanks/ [Accessed 5 October 2021].

Another concrete example of how this understanding is embraced by the law can be found in the Spanish legislation that regulates biomedical research and defines a biobank as 'a public or private non-profit establishment which has a collection of biological samples conceived for biomedical diagnostic or research purposes, and organised as a technical unit with criteria relating to quality, order and destination'[304].

In summary, from this analysis of different official documents and reports, we find that a biobank, as a minimum unit, is defined as an entity or site that collects and organises human biological materials and associated information in the context of biomedical research. I believe this approach corresponds to a first level of understanding, where the definition of biobanks refers primarily to its function as a 'biomedical depository'.[305]

This basic level of understanding of a biobank, which emerged from the legal and ethical normative framework, also reflects the majority of the scientific literature on biobanks. For instance, Hewitt and Watson propose that, given the variety of definitions and the changing usage of the term over time, we should refer to a biobank as:

> A facility for the collection, preservation, storage and supply of biological samples and associated data, which follows standardized operating procedures and provides material for scientific and clinical use.[306]

Important as a shared definition of the term 'biobank' is, I believe that the reality of a biobank is not fully embraced by describing its function; for this reason, we must expand the comprehension of the concept of the biobank beyond its mere function.

b. The biobank as a technoscientific and research infrastructure

The reality of biobanks is not limited to their physical sites, where a set of freezers are kept at the service of biomedical researchers. Indeed, over the years, we have witnessed the shift from small and personal repositories to large-scale biobanks. In particular, they have evolved from an ancillary activity conducted by pathologists, geneticists, microbiologists and other scientists to fuel their own research, to a structured and

[304] Article 3, Ley 14/2007, 3 July, on biomedical research.

[305] Argudo-Portal & Domènech (n 2).

[306] R. Hewitt & P. Watson, 'Defining biobank' (2013) Biopreservation and Biobanking, *11*(5), 309–315, p. 314.

professional activity that is today key in mapping the human genome, delivering personalised medicine in clinics and identifying risk factors of diseases.[307]

As described by Cambon-Thomsen, this transition has been prompted by a combination of many factors:

> technical and computational advances (such as high-throughput genomics techniques), new systematic approaches (including large-scale SNP genotyping to characterize genomic variation), and the growing level of exchange of biological material and information among researchers.[308]

A further, and important, factor needs to be considered when explaining the transition of biobanks from single repositories to technoscientific infrastructures: that this transition occurred at the same time as, and was triggered by, a crucial epistemic change in biomedical research – the new paradigm of big data-driven biomedical research.[309] Specifically, the genetic, genealogical, health and other personal information associated with human biological samples collected by biobanks can be used for a variety of research purposes and, from them, a multitude of different datasets can be extracted. Thus, 'the greatest value comes from these rich resources if they can be combined in the form of "Big Data" for use in addressing research questions of global significance'.[310]

In this regard, the analysis of Hainaut and colleagues is particularly effective: in introducing the challenges of biobanking in the 21st century, it draws a parallel between the expansion of large-scale biobanks and the big data revolution that has affected science in the first decades of this century:

> The 'four V's' of Big Data also apply to Biobanking: volume (scale and number of specimens); velocity (collection and analysis of streams of specimens within very strict time constraints); variety (different types of specimens); and veracity

[307] Hainaut and others, *Biobanking of Human Biospecimens* (Springer International Publishing 2021).

[308] A. Cambon-Thomsen, 'The social and ethical issues of post-genomic human biobanks' (2004) Nature Reviews Genetics, *5*(11), 866–873. p. 867.
[309] K. L. Hoeyer, 'Size matters: the ethical, legal, and social issues surrounding large-scale genetic biobank initiatives' (2012) Norsk Epidemiologi, *21*(2).
[310] D. Chalmers and others, 'Has the biobank bubble burst? Withstanding the challenges for sustainable biobanking in the digital era' (2016) BMC Medical Ethics, *17*(1), 1–14.

> (uncertainty on the preservation status of biomolecules, cells, and tissues within a specimen).[311]

Thus, the combined impulse of technical advances and the emergence of biomedical big data has accelerated the transition towards the large-scale dimension and launched the era of biobanks as technoscientific research infrastructures. As such, in the words of Ho, biobanks are today the first fundamental resource in a research pipeline that aims to understand 'the interaction between genetic factors underlying common complex diseases and the environment, and the translation of biomedical research into diagnostic and therapeutic applications through pharmacogenomics in pursuit of personalized medicine'.[312]

In this sense, biobanks are unique in terms of their position and role. They are located at the thriving intersection between medical science, genomics, genetics, molecular biology and informatics and, at the same time, provide biospecimens and associated data to the scientific community to enable progress in science and medicine.

Thus, as suggested by Madison, biobanks as infrastructures can be also seen as knowledge institutions since:

> They collect, curate and steward biological materials and associated knowledge and information for the benefit of future generations and for present scientific researchers. They house knowledge resources, and they provide important knowledge infrastructure for the production of new knowledge.[313]

In other words, as infrastructures that support biomedical research, biobanks are invested with a double role: on the one hand, the stewardship function that helps to preserve knowledge and data systematically for future generations and, on the other, the production function that supports the generation of new scientific and medical knowledge.

This notion of the biobank extends the understanding of biobanking beyond the collection, storage and delivery of samples and associated data, conferring on it the role of a fundamental support to researchers at different stages of research projects involving the use

[311] Hainaut and others (n 10).
[312] C. H. Ho, 'Challenges of the EU "general data protection regulation" for biobanking and scientific research' (2017) Journal of Law, Information and Science, *25*(1), 84–103.
[313] M. J. Madison, 'Biobanks as knowledge institutions' In *Global Genes, Local Concerns* (Edward Elgar Publishing 2019) 38.

of biological samples and data. It requires the continuous work of ethics committees that assess access requests and services offered by IT platforms up to the level of networks of biobanks involving a transversal organisation and structure.

At this level of understanding, the concept of the biobank no longer refers to a discrete biomedical collection of samples and associated data but one embedded in a complex ecosystem that provides fundamental support to the production of scientific knowledge and faces the challenge of bringing together all the various players involved in this production (i.e. patients, participants, researchers, biobankers, industry, universities, public). Indeed, only having reached the level of infrastructure, can a research biobank express its full potential and make a real difference, as suggested by the Council of Europe's expert group, which claim that, as a research infrastructure, biobanks 'will enable new scientific questions to be rapidly addressed with increasing efficiency'.[314]

In my opinion, two features best reflect this idea of the biobank as a complex ecosystem: the multitude of stakeholders actively or passively involved in the process and the numerous networks that characterise the world of biobanks.

Starting from the stakeholders, given the multiple specific operations and relationships that require the intervention of many different players. In the face of this complexity, the organisation and the sustainability of biobank projects, 'stakeholders' is the appropriate umbrella term for all the individuals involved in setting up, running, using and consulting a biobank. The term belongs to the vocabulary of project management and organisation theory and is defined as a 'person, group or organisation that has interest or concern in an organisation. Stakeholders can affect or be affected by the organisation's actions, objectives and policies.[315]

As noted by Bjugn and Casati,[316] a systematic stakeholder analysis is essential from the earliest planning stages of any biobank project because the more the organisation is aligned with stakeholders' values, interests and expectations, the greater the likelihood of success.

[314] European Commission, Directorate-General for Research and Innovation, *Biobanks for Europe: a challenge for governance* (Publications Office 2012) 8. Available at: https://data.europa.eu/doi/10.2777/68942

[315] J. Post, *Redefining the Corporation: Stakeholder Management and Organizational Wealth* (Stanford University Press 2002).

[316] R. Bjugn & B. Casati, 'Stakeholder analysis: a useful tool for biobank planning', (2012) Biopreservation and Biobanking, *10*(3), 239–244.

The authors applied a project management and organisational theory framework to the field of biobanking, and explain that stakeholder analysis usually includes the following five tasks: '(i) identification, (ii) attributing values, (iii) prioritizing, (iv) devising a plan for engagement, and (v) monitoring'.[317]

Furthermore, an analysis of biobank stakeholders is crucial to understanding the social, cultural and political environment in which the infrastructure is integrated. As observed by Ciaburri and colleagues, it is a form of identity kit that helps to evaluate which of their interests the biobank must protect and which are able to influence the biobank to develop processes that satisfy the expectations of the various stakeholders.[318]

For the sake of my arguments, I shall try to complete the task of identifying the major biobank stakeholders and understanding the values and interests that are associated with each in order to relate to them meaningfully. Since the list of stakeholders can be lengthy and, at the same time, biobank projects can vary greatly in type and composition, I will simply group potential stakeholders into categories containing persons, groups or organisations of a similar nature to provide a general overview valid for any biobank.

Based on a literature review on the topic of biobank stakeholders,[319] I have identified the following main groups, starting from the most 'internal' actors and moving outwards. For each group, I will suggest the interests, values and expectations they bring to the biobanking environment.

- Participants are individuals who give samples and associated data to the biobank. They may be patients in a hospital, people with non-severe health conditions or healthy volunteers. In line with the participatory turn in biomedical research,[320] I will refer to this group of stakeholders with the general term 'participants', for various reasons. First, it is an umbrella term that includes patients – those individuals in a hospital context who agree to let their biological materials and data be used for research purposes (disease-oriented biobanks) – and all those who accept an invitation to participate in research projects and epistemological studies (population-

[317] Ivi, p. 239.
[318] Ciaburri, Napolitano & Bravo (n 107).
[319] Bjugn & Casati (n 119); Ciaburri, Napolitano & Bravo (n 107);
C. Klingler and others, 'Stakeholder engagement to ensure the sustainability of biobanks: a survey of potential users of biobank services', (2021) European Journal of Human Genetics, 1–11.
[320] J. Kaye and others, 'From patients to partners: participant-centric initiatives in biomedical research', (2012) Nature Reviews Genetics, *13*(5), 371–376.

based biobanks). Secondly, I prefer the term 'participants' to 'donors' or 'research subjects' because it emphasises the concrete possibility of those individuals being meaningfully involved in a biobank project rather than treated as passive actors.[321] In particular, I believe that vocabulary from the semantic sphere of donation and gifts should be dismissed in relation to biobanking in favour of one emphasising the value of participation and solidarity.[322] The interests of this group of biobank stakeholders depend on whether they are patients or individuals participating in a biobank project. The former may have an interest in allowing their samples and data to be used in a research project that will eventually benefit themselves with the development of new diagnoses and treatments, or may benefit other patients with the same diagnosis in the future. The latter's interest in participating may be driven by an altruistic wish to contribute to the advancement of research and its prompt impact on the healthcare system.

- Researchers are the real users of biobanks as they require access to biobanked samples and associated data to advance their research projects. They may be part of an internal research group at a public or private institute or hospital where the biobank is hosted or from a public or private external institution. Generally, researchers approach a biobank through its online catalogue and submit a material/data transfer agreement with it. Researchers' interest in the biobank project is easily attributable to the need for high-quality and well-annotated human biological materials to progress their research. How access to the biobank resources is regulated (i.e. allocation and priority-setting policy) deeply affects them and their research project. Conversely, biobanks rely strongly on researchers' requests to become effective and increase their visibility and reputation in the scientific community.

- The biobank staff includes both the biobank personnel listed in the organisational chart of each biobank (i.e. the biobank director, head of core facilities or operational manager, laboratory technicians, informed consent manager) and the external personnel involved in the daily processes of the collection, storage and distribution of

[321] K. Saha & J. B Hurlbut, 'Research ethics: Treat donors as partners in biobank research' (2011) Nature, 478(7369), 312; A Buyx and others, 'Every participant is a PI. Citizen science and participatory governance in population studies' (2012) International Journal of Epidemiology, 46(2), 377–384.
[322] L. Locock & A. M. R. Boylan, 'Biosamples as gifts? How participants in biobanking projects talk about donation', (2016) Health Expectations, *19*(4), 805–816.

bioresources (i.e. clinicians, geneticists, epidemiologists, nurses and other medical and administrative staff). To this list must be added the members of the scientific and ethics committees who, as we will see in the following paragraphs, play a key role in biobank governance. They are usually researchers, bioethicists, ELSI (ethical, legal and social issues) experts, etc. Taking account of the needs of this group of stakeholders in terms of the functioning of the biobanking processes, and listening to their requests, is essential to the success of a biobank project, especially in light of the fact that biobank staff and external personnel often perform tasks related to the biobank in addition to their regular employment as researchers, clinicians, laboratory technicians, nurses, ethics experts, etc. In other words, they usually agree to perform highly specialised work for the biobank as an in-kind contribution.

- Disease-focused foundations and patient organisations are usually not-for-profit entities that are patient- or disease-focused, and in which patients and patient representatives represent the majority of members of the governing bodies.[323] The involvement of these bodies in biobanking is driven by the will of patients and their representatives to be part of the decision-making governance structure of biobanks in order to express their perspectives and expectations on how their samples and data are used and distributed.[324] Accordingly, this group of biobank stakeholders has an interest in ensuring that biobanking policies and decision-making processes better safeguard patients' rights and concerns. At the same time, the commitment of this group of stakeholders to the biobank is essential for its viability, as they can influence patients to participate or not in a biobank project.

- Public institutions or bodies are represented in the biobanking field by the State, the region, the municipality or the hosting public institution (hospital or university). They are fundamental stakeholders as they define the legislation on which the existence of the biobank is based and, in the case of public institutions, the official accreditation of a biobank. Furthermore, they usually provide partial or total funding for biobanks. Accordingly, the nature of their interests varies, ranging from the allocation of finances for biomedical research, to the level of regulatory openness in terms of

[323] D. Mitchell and others, 'Biobanking from the patient perspective' (2015), Res Involvem Engagem, 1:4.
[324] C. Baldo and others, 'The alliance between genetic biobanks and patient organisations: The experience of the Telethon Network of Genetic Biobanks' (2016) Orphanet J Rare Dis, 11:142.

participants' protection, to the balance between local research needs and international networking.

- Private sector and partners: pharmaceutical and biotechnology companies rely on biobanks' bioresources to develop their commercial products and, for this reason, they are biobank stakeholders. Partnerships between public and private sectors in the field of biobanking are not to be rejected, yet they raise multiple issues, in particular regarding possible conflicts of interest that may emerge in the meeting of a public field built on altruism (biobank participation) and the private sector driven by market values. They can also play a funding role.

- Society: society itself is a crucial stakeholder as it represents the 'final recipient' of the benefit generated by biobanks. This group includes all the aforementioned stakeholders but, at the same time, is broader since it encompasses citizens as a whole. In what follows, I will also refer to this stakeholder group as 'the public'. The interest of society in biobank projects is two-fold. First, in a public health system, there is a need for research goals to be aligned with the expectations of research users and, therefore, to be impactful. Secondly, the viability of a biobank depends on fostering trust and support from the public through transparent communication and engagement activities.

Moving to the networks, in their role as a supporting tool for biomedical research, biobanks need to collaborate both at national and international levels in order to effect a real impact and make the transition from a local research tool to a complex international research infrastructure. This type of thriving collaboration is currently achieved in Europe in two ways: international infrastructures and national networks of biobanks. Their establishment was driven by two main problems that commonly prevent the adequate flow of biobank resources: i) the heterogeneity of biobanking due to the fact that samples and data are often collected under different legal regulations and technical standards, ii) the lack of clear guidelines on ethical and legal challenges.

Accordingly, international research infrastructures for biobanking play a key role in facilitating the standardisation of procedures and management and support with ethical and legal issues. I will now present three successful cases in order of appearance.

The International Society for Biological and Environmental Repositories (ISBER)[325] was established in 1999 with the aim to facilitate and promote networking between biobanks and 'to share successful strategies on providing fit-for-purpose specimens for research and to develop harmonised principles in the science and management of repositories'.[326] Accordingly, it is committed to periodically issue and improve upon 'ISBER Best Practices: Recommendations for Repositories' which reports on the most up-to-date procedures regarding the quality management of biospecimens and provides guidelines and standards for the most common ethical and legal issues.

The European, Middle Eastern and African Society for Biopreservation and Biobanking (ESBB)[327] was founded in 2010 with the mission of empowering biospecimen sharing among different countries by building and educating a strong biobank community. It does so through extensive education and training programmes, annual conferences, working groups and task forces.

The Biobanking and Biomolecular Resources Research Infrastructure (BBMRI)[328] was proposed in 2006 at the European Strategy Forum on Research Infrastructures (ESFRI) and, after an exploratory phase, supported by the European Commission from 2008 to 2011.[329] In 2013, it officially became an ERIC (European Research Infrastructure Consortium),[330] that is, a specific legal form that facilitates the establishment and operation of research infrastructures with European interests.

BBMRI-ERIC today comprises 28 European member states (national nodes) and its role is to manage the directory of partner biobanks (i.e. an IT tool that facilitates access to quality-controlled biospecimens and associated data stored in biobanks). In addition, it offers support to biobanks in terms of quality management, information technology, ethical, legal and societal issues, GDPR and a number of online tools and software solutions.

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[325] ISBER - International Society for Biological and Environmental Repositories. https:// www. isber. org/ Accessed 2 Feb 2022.
[326] L. D. Campbell and others, 'The 2018 revision of the ISBER best practices: summary of changes and the editorial team's development process', (2018) Biopreservation and Biobanking, *16*(1), 3–6.
[327] European, Middle Eastern & African Society for Biopreservation and Biobanking. https:// esbb. org/ Accessed 3 Feb 2022.
[328] Home | BBMRI-ERIC: making new treatments possible. https://www. bbmri- eric. eu/ Accessed 3 Feb 2022.
[329] Final Report Summary - BBMRI (Biobanking and biomolecular resources research infrastructure) - report summary - FP7 - CORDIS - European Commission. https:// cordis. europa. eu/ project/ id/ 212111/ repor ting Accessed 3 Feb 2022.
[330] European Commission – ERIC. https://ec.europa.eu/info/research-and-innovation/strategy/strategy-2020-2024/our-digital-future/european-research-infrastructures/eric_e Accessed 3 Feb 2022.

To sum up this overview, some common features are worth noting. International biobank infrastructures share a common aim to foster and educate a biobank community in order to bring together the many players and stakeholders that constitute this field: the biobank, industry partners, patient organisations, the general public, academic institutions and sponsors. Furthermore, they are committed to working towards the technical, legal and ethical harmonisation of practices crucial to facilitating biospecimen and associated data sharing in order to maximise the impact of biobanking on biomedical research.

Alongside these international infrastructures, various national networks of biobanks carry out the same tasks and goals at the micro-level. We will now look closely at one Spanish and one Italian example.

The Spanish Biobank Network (RNBB)[331] is an initiative of the Carlos III Institute of Health in Madrid, formed by 39 Spanish biobanks. It was established in 2009 to facilitate access to human biological samples and data through a common sample catalogue and high-quality scientific and technical support. The added value of the RNBB is the integration of a pool of resources and knowledge of 39 biobanks that help to handle requests for samples that would be difficult for any single entity to meet, such as projects on unrepresentative pathologies, projects requiring a very large number of samples and multicentre projects that need standardised procedures.

Similarly, the *Telethon Network of Genetic Biobanks* (TNGB)[332] is an Italian network composed of 11 Italian biobanks, founded in 2007 under the framework of a research project financially supported by Fondazione Telethon, an Italian charity foundation. The network interconnects already well-established genetic biobanks through a unique and centrally coordinated IT infrastructure designed to respond to the highest quality standards, according to rigorous ethical principles complying with Italian laws and international recommendations.[333]

[331] Home | Red Biobancos. https://redbiobancos.es/en/ Accessed 3 Feb 2022.
[332] Telethon Network of Genetic Biobanks. http://biobanknetwork.telethon.it/ Accessed 3 Feb 2022.
[333] M. Filocamo and others, 'Telethon Network of Genetic Biobanks: a key service for diagnosis and research on rare diseases', (2013) Orphanet Journal of Rare Diseases, *8*(1), 1–11.

c. The biobank as a vantage point for contemporary biomedical research governance

The growing size of collections and the infrastructural transition have increased biobanks' scientific value. This new exposure has, as a primary consequence, opened and extended the discussion on biobanks to new questions such as the relationship between science and society, responsible research and innovation, and issues pertaining to governance, ethics, the law and societal values related to biobanking practice.[334]

As a secondary consequence, the new status of biobanks, as specialist and centralised infrastructures, has in the last decade enhanced their potential to contribute to the process of rethinking and rebuilding practices in biomedical research and healthcare. In particular, their role as resource and service providers can foster translational biomedical research and ultimately the development of personalised medicine; thus, we can agree with Gottweis and Peterson that 'biobanks incorporate visions for the future of medicine and healthcare'.[335] In other words, discussing the ethical implications of biobanks is important not only for the sake of biobank governance itself, but also to lay the groundwork for the future development of biomedical research.

The same conclusion is drawn by Budimir and colleagues, who see in the ethical development of biobanks a form of promise for the future of medicine:

> The future will inevitably bring personalized medicine, which will share a number of similarities with the contemporary biobanks – [there is a] need to protect sensitive information, levels of accessibility, the need to prevent data misuse, and the possibility to predict individual health-related outcomes based on the genomic information.[336]

Based on the above considerations, I argue that, as the carriers of a future vision, biobanks represent a unique opportunity to reassess our approach to biomedical research in the digital era, because there are several points in common between the activities, challenges

[334] V. Argudo-Portal & M. Domenech 'Ethical, legal and social issues publications on biobanks 2011-2018. A scoping review' (2020) Revista Espanola de Salud Publica, *94*.
[335] H. Gottweis & A. Petersen, 'Biobanks and governance: an introduction' in *Biobanks: governance in comparative perspective* (Routledge 2008) 16.

[336] B. Dudimir and others, 'Ethical aspects of human biobanks: a systematic review' (2011) Croatian Medical Journal, *52*(3), 262–279. p. 273.

and needs of biobanking practice and biomedical research practice more generally. As such, we can argue that the relationship between biobanking and biomedical research is that which exists between the micro and macro levels of the same reality. Therefore, having embraced this conceptual understanding of the biobank, I defend its vision as an unmissable opportunity to improve the ethical governance of biomedical research in the digital age.

We should, however, also note the negative aspects of this promising prediction regarding biobank governance. As mentioned by Gottweis and Peterson, the risk is that biobanks will act like 'machine(s) to make a future'.[337] While it is true that we can rely on biobanks as biomedical infrastructures with a broad field of application and potential, we should not load them with the expectation of answering questions that researchers themselves are not still able to clearly express. Currently, many objectives achievable through biobanking, as well as the precise strategies to reach them, remain relatively vague.

In conclusion, the widespread narrative of biobanking as a force to change the future of medicine and healthcare brings at the same time both opportunity and risk. The challenge is to keep the narrative aligned with the development of the reality.

The opportunity in my opinion is to take advantage on the reflection on biobank governance today to develop some of the most crucial questions in the ethics and regulation of data-driven biomedical research that can be summarized as follow. What is the best way to regulate the collection, use and sharing of human biological samples and associated health and personal data? How can we achieve harmonisation, in terms of best practice and ethical guidelines, in order to implement international sample- and data-sharing and preserve participants' rights? How do we regulate and manage the role of the biobank as the steward of samples and data and, at the same time, a facilitator for resource-sharing? How can we manage and make all stakeholders aware of the fluidity between biobanks and large-scale bioinformatic datasets and, more generally, of the fact that data today extend far beyond the sample itself? What kind of future for biomedical research and healthcare can biobanks convey? What is the most desirable scenario for all the stakeholders involved (patients, participants, researchers, clinicians, funders, the pharmaceutical industry and universities)? How do we translate ethical principles into actions in everyday practice?

[337] Gottweis & Petersen (n 19).

d. The biobank as a testing ground for revising ethics in biomedical research

To introduce this fourth level of understanding the biobank, I turn to the words of Nathaniel Comfort in an article written for the 150th anniversary of *Nature*. In retracing the history of how advances in biomedical research and biotechnology have shifted our sense of identity, the author maintains that, in recent years,

> Cell and molecular studies have relaxed the borders of the self. Reproductive technology, genetic engineering and synthetic biology have made human nature more malleable, epigenetics and microbiology complicate notions of individuality and autonomy, and biotechnology and information technology suggest a world where the self is distributed, dispersed, atomized.[338]

Accordingly, given that biobanks are today the meeting point of all these disciplines, we should not be surprised that the discussion on biobank governance produces a highly complex set of bioethical reflections. To give just some examples: genetics brings the issues of scientism and determinism; the use of biotechnologies carries the burden of fair and ethical regulation; data-intensive biomedical research comes with the difficulty of protecting individual rights to autonomy and privacy. Moreover, these are only general issues related to scientific disciplines.

I argue that, in line with this level of understanding of the phenomenon, biobank governance can be described as a testing ground for rethinking the research ethics framework in the face of the challenges of the digital era and, in turn, for proposing updated principles to protect research participants. In addition, I maintain that, from this perspective, the biobank is the reality where many contemporary bioethical subjects of discussion, related to data, biotechnology and health converge, in particular those related to the secondary uses of genetics and personal information in biomedical research.[339]

In my opinion, reflection on biobank governance not only extends the discussion to innovative and promising scenarios of research and healthcare, but offers a valuable opportunity to look at a crucial and timely imperative in the field of biomedical research: the ethical and social impact of scientific knowledge, communication of such knowledge and its

[338] N. Comfort, 'How science has shifted our sense of identity' (2019) Nature, *574*(7777), 167–170, p.168.
[339] R. Anderson, 'The collection, linking and use of data in biomedical research and health care: ethical issues' (2015). https://doi.org/10.17863/CAM.31760

delivery in society.[340] As such, biobanks can be seen as a public arena, implementing public engagement and participation and, ultimately, as a fertile ground for testing a new relationship between science and society.[341]

At the same time, using the words of Hoyer, a biobank is 'an arena for public contemplation of issues'.[342] This means that, from a bioethical perspective, in discussing the ethical challenges related to biobanks' secondary uses of samples and data, we have at the same time an opportunity to bring to the attention of a large number of stakeholders – both experts and lay public – the crucial ethical questions that characterise biomedical research and innovation, such as data protection, the commodification and commercialisation of human body parts and the relationship between public and private sector.

Based on these considerations, effective biobank governance in the digital era must take advantage of the following two opportunities, to which I aim to contribute with this dissertation. First, if the biobank is an arena for implementing a new relationship between science and society, then biobank governance must understand in depth what the concepts of participation, involvement and empowerment mean in this context, and how to implement them. Then, we can start to think of the practice: how both participants and society can be empowered by their involvement in research biobanks and how individuals can construct their positioning in it and legitimate their rights.

Secondly, embracing the concept of the biobank as an arena for the public contemplation of issues offers an opportunity for biobank governance to foster mechanisms of public engagement aimed to raise awareness of ethical issues related to this practice in the context of data-driven biomedical research. In particular, we have the opportunity to test new and timely principles to guide biobanking practice, rather than relying only on the traditional, paternalistic and human-rights-based paradigms of medical research ethics. Promoting the conceptualisation of updated ethical principles – transparency, data protection and participation – may eventually help to make the practice of biobanking more ethical, beyond the mere application of the law, and result in empowering individuals through a transparent dialogue and the opportunity to scrutinise governance mechanisms.

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[340] M. Casado & P. Puigdomènech (eds.) *Documento sobre los aspectos éticos del diálogo entre ciencia y sociedad* (Edicions de la Universitat de Barcelona 2018) ISBN 978-84-9168-100-7. Available at:
[341] S. Casati, M. Tallacchini & F. Bonino, 'Governance e salute: un laboratorio tra ricerca e cura' (2006) *Notizie di Politeia*.
[342] Hoeyer (n 12).

2.2. From a medical oriented to a societal oriented vision of biobank

An effective model of governance for biobanks in the digital age needs to embrace a broad vision of the biobank, encompassing an understanding of the biobank as a viewpoint for the challenges of biomedical research and as a testing ground to improve research ethics.

As seen in the previous chapters, the difficulty of navigating new challenges with unsuitable ethical guidance appears to have reached an impasse, and many issues regarding biobank participation and the management of sample and associated data collections remain unresolved. Accordingly, in order to progress towards a conceptualisation of an appropriate governance model for biobanking in the digital age, I propose to look at the question differently.

As a result of applying the above framework to the concept of the biobank, we can separate the understandings of biobanks into two different models. As I will argue below, it is precisely in the transition from the first to the second vision of biobanks that the possibility of a turning point lies, both in theory and in practice, in terms of rethinking the governance of such realities.

For the purposes of this argument, I will use the flow of samples and associated data in biobanks as the context against which I will compare the narrow and broader visions of the biobank. There are, in my opinion, three crucial stages that biobank governance should address in the everyday practice of biobanks. Each of these is associated with specific actions which, in turn, are associated with specific ELSI.

i) From the needle to the freezer. This stage usually takes place in a clinical setting or hospital and ends with placing the samples in the location designed for the freezers. Several actions and procedures are involved here: obtaining informed consent, the extraction of the sample, quality and safety procedures during the biobanking activity itself and the generation of data sets.

ii) From the freezer to the labs. This includes all the procedures put in place for sample- and data-sharing within the scientific community. More precisely, it starts from the moment in which an external researcher applies for biobank samples and associated data, and continues until they are shipped to the final recipient. It

includes access request procedures, the evaluation of requests by the designated committee, transfer agreements between the parties involved and safe shipment with all appropriate safety measures.

iii) From the labs to society. This concerns the strategies and procedures for giving results from the biobank to participants, to the biobank from the researchers that have received samples and data, and to the scientific community and general public from the researchers and the biobank. In particular, this stage is where the relationships with external partners and stakeholders are fostered, with the presumed goals of ensuring and sustaining public trust, increasing public engagement and promoting participant involvement and empowerment.

A narrow vision of biobanks derives from the traditional ethical research framework and leads to a deadlock, where the limits of the current governance structure of biobanks and ethical principles appear insurmountable.

In particular, this narrow vision of biobanks is conveyed by an understanding of the biobank merely as a collection of samples and data and an infrastructure to accommodate the needs of the scientific community. This understanding of biobanks is very conventional, in the sense that it reflects how biomedical research involving human subjects has been understood and approached by research ethics. Therefore, it can be argued that this model is medical-oriented; it is conceived by placing researchers and scientific progress at the heart of the system. Of course, the participant – who gives samples and data for research purposes – is not neglected, and substantial efforts are made to protect their rights, but the centre stage is occupied by other, more cumbersome, players. Indeed, as this model highlights the concrete function of a biobank – collecting, storing and providing biospecimens and associated data for biomedical research – it goes without saying that the researchers are centre-stage as privileged recipients. Alongside them stand the host or funding institution (e.g. university or hospital) and the biobank staff (biobank directors, lab technicians, administrative department, scientific and ethics committees).

This narrow vision of the biobank is too individual-centric. The focus is always on controlling individual activity (in the case of the researcher) or protecting individual rights (in the case of the research participant). Little attention is given to the benefit-sharing that comes from biobanking, its implications for health care and its impact on society and citizens' empowerment.

At the level of practice, in this narrow vision, the concrete activity carried out in a biobank every day is very similar to that performed in other scientific contexts, such as universities, hospitals, public or private research institutes, where basic research, clinical trials and laboratory investigations take place. These activities are mainly those related to the first two stages of samples and data flow in the biobank described above – from the needle to the freezers, and from the freezers to the labs – and they follow long-established practical protocols and ethics guidelines.

According to this narrow vision of the biobank, which sees biobanking activities merely as branches of biomedical research, we can assume that many features, challenges and issues present in biobanking practice may respond to strategies, guidelines and approaches that are well-established and widely accepted in the domain of biomedical research.

The narrow vision of the biobank is the one that has to date been embraced by the international ethical-legal framework applied to biomedical research and biobanks. As explained in Chapter 2, the traditional ethical framework originated as a result of the many abuses carried out in the name of medical research during and in the aftermath of World War II. Over time, the ethical and legal framework that resulted from, the Helsinki Declaration of the World Medical Association, the Council of Europe's Convention on Human Rights and Biomedicine, and UNESCO's Universal Declaration on Bioethics and Human Rights has become the universal reference point when talking about biomedical research ethics and the duties of clinicians and investigators towards patients, donors and research participants.

However, as demonstrated in Chapter 2, the principles and applications coming from this framework has proved to be inadequate to cope with the ethical challenges brought by the digital paradigm in biomedical research. Therefore, to support my argument that a narrow vision of biobanks, based on the traditional research ethics framework, is not able to inform the conceptualisation of an effective governance model in data-driven biomedical research, I compare the principles of the World Medical Association's Declaration of Helsinki – the most cited document on international guidance in research ethics – with those most recurrent in biobanks' ELSI, namely privacy, informed consent and secondary uses, in order to demonstrate the conflict between the challenges faced by biobanks in the digital era and the research ethics framework.

The Declaration of Helsinki, developed in 1964 by the World Medical Association, is a statement of the core ethical principles governing biomedical research. It provides concise

guidance to medical practitioners and researchers on all aspects of research involving humans, identifiable human biological material and associated data. As such, it regards biobanks as repositories of samples and associated data.

It focuses on the importance of protecting the dignity, autonomy, privacy and confidentiality of research subjects, and obtaining informed consent to use identifiable human biological material and data. At the heart of the document, indeed, is the requirement to inform potential subjects about the proposed research, and to obtain their consent before the research is carried out (Art. 25–32). In particular, Art. 32 states:

> For medical research using identifiable human material or data, such as research on material or data contained in biobanks or similar repositories, physicians must seek informed consent for its collection, storage and/or reuse. There may be exceptional situations where consent would be impossible or impracticable to obtain for such research. In such situations the research may be done only after consideration and approval of a research ethics committee[343].

This is the only direct reference to biobank research in the entire document and is emblematic of its narrow and medical oriented vision of biobanks – it provides guidance for physicians, not for researchers handling the collected samples and data, and the reference to the approval of RECs regards only cases where it is impossible to obtain consent. Yet, the specific challenges faced by biobank governance, namely the incompatibility of specific consent for samples and data collected for future research and the loss of control experienced by participants, undermining their dignity and autonomy, are not contemplated. Moreover, the narrow vision of the biobank contemplated by the Declaration of Helsinki is not compatible with the novel ethical, legal and social issues raised by data-intensive biomedical research, such as the re-use and re-purposing of personal data, unwanted uses and commercialisation of biobank resources, and risks related to the possibility of the re-identification of personal data.

[343] World Medical Association. 'World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects' (27 Nov 2013. Available at: https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/

In conclusion, this narrow understanding of the biobank, conditional on medical needs and embedded in the research ethics framework, is not adequate to express the potential of biobanks.

In contrast to the scenario described above, I defend a broad vision of the biobank, based on an understanding of it as a vantage point for the challenges of biomedical research in the digital age and as a testing ground for implementing research ethics. I argue that a societal and participatory understanding of the biobank is needed to overcome the limits of the current ethical framework for biobank governance. In addition, a broader vision of biobanks will also make possible the implementation of the concept of governance, ethics and public engagement presented in the EU Responsible Research and Innovation framework (RRI) in the context of biobanks.[344]

If the narrow vision of biobanks is medically oriented, the broader one that I propose is, in contrast, societal oriented, since it accommodates the need for, on the one hand, public and participant engagement in line with RRI principles and, on the other, a greater focus on data protection which has been identified as a priority for protecting research participants in the context of data-driven biomedical research.

Shifting the attention from the single individual (researcher, patient or physician) to all those involved in biobanking and to all the procedures involved, including those before and after the moment of collection and storing of samples and associated data, allows the right space to be given to those stakeholders usually left out of the conventional narrative surrounding this topic: the participants, patient advocates and associations, scientific and ethics committees, and society. Accordingly, it creates space for biobank governance to comply with those dimensions considered crucial for RRI: diversity and inclusion, openness and transparency.

Thus, when we embrace this broad vision of the biobank, the first positive consequence is that the cluster of actions enclosed in the stage labelled ‘From labs to society’ is unlocked, and the neglected questions automatically become objects of consideration. I refer here to procedures for returning scientific results to participants from the biobank, including dealing

[344] Regulation (EU) No 1291/2013 of the European Parliament and of the Council of 11 December 2013 establishing Horizon 2020 - the Framework Programme for Research and Innovation (2014–2020) and repealing Decision No 1982/2006/EC Text with EEA relevance; M. Casado and others (n 30).

with incidental findings, the relationship between the biobank and the researchers who have received samples and data and the broad relationship between the biobank, the scientific community and general public. Therefore, a broader vision of biobank, societal oriented and open towards public engagement places great relevance on relationships with the outside and all the stakeholders are fostered with the presumed goals of ensuring and sustaining public trust, increasing public engagement and promoting participant involvement and empowerment.

The focus on the future and society embraced by a broader vision of biobanks is the right way to look at the question of effective governance for biobanks and data-driven biomedical research. However, we must be careful not to abandon the strengths of the previous system. To be sustainable and trusted, this model of biobank governance needs to be supported by an ethical framework that is just as strong and reliable as the previous one has been over a period of decades.

It must be acknowledged that, in the somewhat unpromising scenario described, a step forward seems to have been made by the Declaration of Taipei on Ethical Considerations Regarding Health Databases and Biobanks (hereinafter the Taipei Declaration), adopted in 2002 and revised in 2016 by the World Medical Association.[345] The most recent version of the Taipei Declaration is intended to cover the collection, storage and use of identifiable data and biological material beyond the individual care of patients and is intended as an extension of the Helsinki Declaration, providing additional ethical principles for use in Health Databases and Biobanks. In particular, it lists a set of principles upon which the governance of health databases and biobanks must be built:

i) The protection of individuals: governance mechanisms should be designed so the rights of individuals prevail over the interests of other stakeholders and science;
ii) Transparency: any relevant information on health databases and biobanks must be made available to the public;
iii) Participation and inclusion: custodians of health databases and biobanks must consult and engage with individuals and their communities;

[345]World Medical Association. 'World Medical Association Declaration of Taipei: on ethical considerations regarding health databases and biobanks' (12 Oct 2016). Available at: https://www.wma.net/policies-post/wma-declaration-of-taipei-on-ethical-considerations-regarding-health-databases-and-biobanks/

iv) Accountability: custodians of health databases and biobanks must be accessible and responsive to all stakeholders.

As regards my arguments, the Taipei Declaration represents an important reference point as ethical guidance that adopts a broader vision of biobanks, looking at the issues and challenges from an appropriate perspective. At the same time, it is important to note that the Declaration does not simply dismiss the ethical principles that form the cornerstones of the old ethical framework, but integrates them and elaborates on them. Indeed, the Taipei Declaration is based on respect for the rights to dignity, autonomy, privacy, precisely those that enable biobank participants to exercise control over the use of their biological samples and associated personal data. In addition, confidentiality is intended, as an essential element in maintaining trust in and the sustainability of biobanks.

Aicardi and colleagues have emphasised the overarching goal of this Declaration of protecting people against harms arising from research, with a focus on how research is conducted today and the role of research participants; thus, it does refer to the data-intensive environment. However, the authors are rightly concerned about the fact that 'changing practices in the collection and use of digital data require a revised framework and nomenclature regarding the norms, rules, and principles governing biomedical research'.[346] In other words, it can be argued that, while valuable efforts have been made to codify ethical principles for the use of data in health databases and human biological material in biobanks, given the pervasiveness of biomedical big data – few steps have been made to explain and deepen protection, transparency, participation and inclusion in the context of biobanks, given the specific features and challenges of the digital paradigm.

In conclusion, the Taipei Declaration does look at the question of biobank governance in a digital society from the right perspective, trying to provide updated ethical principles. However, it fails in clarifying them as can be seen in its description of the principle of transparency, which is limited to stating that 'any relevant information on health databases and biobanks must be made available to the public'. To be impactful, the codification of the principle of transparency for biobank governance in the digital era must specify the information that the public and participants actually need to interact appropriately and effectively. The same applies to other principles – what are the scope and accountability mechanisms in biobanking? What are adequate measures to protect participants and their

[346] ibid.

data in research biobanks? What are the concrete risks in everyday biobanking practice that the public and participants should be aware of?[347]

A new ethical perspective that adequately supports the broader vision of the biobank and all its challenges is currently missing, and I aim to contribute to filling this gap. First, however, I shall present arguments in support of the claim that a model of biobank governance that relies on a broader vision of the biobank, oriented towards society and participation is the best way to approach the conceptualisation of biobank governance in the digital era.

Firstly, biobanks at the micro-level and biomedical research at the macro level must grasp the opportunities brought by the digital era, namely the collection, integration and use of multidimensional personal datasets from different sources that have a significant scientific value. As noted by Gille and colleagues, 'biobanks are thus bound to be a key node not only of a rapidly increasing health data ecosystem, but also of an ever-more complex governance network'.[348] In response to the increasing and diversifying volumes of data in biomedical research, I maintain that the sustainable and ethical governance of research biobanks can accommodate the new research paradigms (precision medicine, digital health, etc.) and, at the same time, appropriately address the challenges (broad consent, secondary uses, data protection and participation), ensuring alignment with participants' rights and society's values and expectations.

Secondly, it is important to stress that only by embracing this broader vision of biobank can we conceptualise a model for governance that accommodates all the possibilities encompassed in the future directions of data-driven biomedical research. These possibilities are succinctly summarised by Gottweis and Peterson as follows:

> [Biobanks] articulate particular rationalities and constitute a complex process of representing science, bodies, medicine and technology. […] Biobanks always connect with society, culture, the economy and politics. Biobanks incorporate visions for the future of medicine and healthcare, offer resources to medical research, suggest particular interactions between medical research and the pharmaceutical

[347] F. Gille, E. Vayena & A. Blasimme, 'Future-proofing biobanks' governance' (2020) *European Journal of Human Genetics*, 1–8.
[348] ivi p. 2.

> industry and embed images of the patient, the citizen, collective identity and society.[349]

Thus, I believe that a good model of biobank governance in the digital society should find a way to respect and combine these aspects; the move from a narrow to a broad vision of the biobank is the first step towards this goal.

Thirdly, embracing a broad vision of biobanks allows space for the implementation of the RRI agenda. As explained in Chapter 1, the concept of 'governance' within the RRI agenda is understood as the structure for implementing RRI within any entity involved in research and innovation. Biobanks are actively involved in this process since, increasingly, biomedicine innovations are derived from biobank samples and data. As reported by Yu, one of the principal problems with the implementation of RRI in biobanking is related to the fact that:

> The general public is often opposed to the idea of commercialization in the field of biomedical research, [..] without truly understanding the process involved in translating discoveries into new innovations and making them safe and available for the benefit of the public.[350]

This lack of understanding on the part of the public and the fear of biobank participants that they are not protected is 'precisely what makes it so difficult for public policy and strategies to be implemented with respect to the commercialization of biomedical innovations derived from biobank samples and data'.[351] Therefore, the way in which the governance of biobanks is designed profoundly affects how both participants and wider society value the commercialisation of research discoveries.

I believe that an appropriate model of biobank governance should ensure protection against the commodification of participants' samples and data, without preventing the translation of discoveries deriving from biobank samples and data into biomedical innovations.

[349] Gottweis & Petersen (n 19).
[350] H. Yu, 'Redefining responsible research and innovation for the advancement of biobanking and biomedical research' (2016) Journal of Law and the Biosciences, *3*(3), 611–635.
[351] ibid.

3. *Pars construens*: The conceptualisation of the model

On a conceptual level, the next step along the path to adequate governance of biobanks in the digital era is to decide where to place the focus. Indeed, having adopted the broad vision of the biobank, the vantage viewpoint that enables us to understand how data-driven biomedical research should be governed and provides a testing ground for revising research ethics to face the digital paradigm, it is now time to embrace a shift in the direction from which we approach the question.

To this end, I suggest identifying what is missing in the research ethical framework and at the limits of the narrow vision of the biobank and its governance structure.

3.1. The focus shift: from a researcher – sample to a participant – data model

I argue that there are two main limits to the current approach, in line with arguments presented in the previous chapters: 1) we do not focus on the participant but predominantly on the researcher and, in turn, on the progress of science; 2) we do not focus on data governance because the ethical and legal approaches to biobanks are mostly sample-centred. For the above reasons, the governance focus is not where it should be and, thus, we keep looking in the wrong direction. It is for this reason that the ethical guidance is inadequate and cannot move forward, even in the case of the Taipei Declaration, which represents the most advanced ethical reference in terms of biobank governance in a data-driven biomedical research context.

Therefore, to implement a model of biobank governance that is well-suited to tackle the challenges of the digital age, we need a focus shift – from a researcher-sample model to a participant-data model.

I maintain that this focus shift should consist of a ‘Copernican Revolution’ in biobank governance. This well-known analogy, used by Kant in the Critique of Pure Reason to reverse the traditional relationship between subject and object in the theory of knowledge, can help explain the scope of the focus shift that I propose. Copernicus made his revolution by discovering that the earth revolves around the sun, rather than the opposite view held by

his contemporaries. Similarly, Kant claimed that it is the subject – the individual human being – that is central in knowledge, not the object, the natural objects outside the subject:

> It is representation [the subject] that makes the object possible rather than the object that makes the representation possible. This introduced the human mind [the subject] as an active originator of experience rather than just a passive recipient of perception.[352]

In the cases of both Copernicus and Kant, the shift in perspective of the observer[353] has provided the dynamic for a new way of thinking and framing the question.

Applying the same analogy to our case, I argue that the current focus on the researcher-sample pair in discussing biobank governance prevents a clear view of all the ethically central questions at stake. Only a shift in the perspective of the observer will provide a new model for sustainable and ethical governance of research biobanks in the digital era. In other words, while we keep the researcher-sample duo at the heart of biobanking activity and discussion, we will continue to neglect the protection of participants' data in data-driven biomedical research, and the benefit-sharing of research and innovation from biobanks within society.

Therefore, the Copernican revolution in our case would apply from the moment we decide to change the focus and look beyond the researcher-sample pairing. The new focus on a participant-data pair will finally include in the picture what has been excluded so far:

- The biobank's users: participants.
- The beneficiary of the research and innovation derived from biobanks: society.
- The centrality of data.

This shift in perspective, even if not comparable to the Copernican revolution in astronomy or the Kantian one in metaphysics in terms of scope and innovation, is crucial for our micro-goal because it allows the right questions to be asked. Indeed, only now – with this focus – do the crucial questions raised by digital society in the context of biobanks emerge: what

[352] I. Van de Poel & L. Royakkers, *Ethics, technology, and engineering: An introduction* (John Wiley & Sons 2011).
[353] N. Colleran, *Immanuel Kant's reference to the Copernican Revolution* (ResearchGate preprint October 2019).

can and cannot be done with the samples and personal data collected by biobanks? What research can and should be done to achieve social benefit? What is the right way to protect biobank participants' samples and data against the trend toward commodification?

Moreover, only with this new focus in mind is it possible to explain why the ethical guidance traditionally applied in the 'researcher-sample' approach to biomedical research and biobanks is no longer applicable or effective: it does not see the problems and challenges because it is looking in the wrong direction.

In conclusion, I believe that this shift of focus has the merit of better accommodating the new challenges faced by biobank governance today (i.e. the transition from a sample-centric to a data-centric research environment, assurances on data protection, promoting public engagement, engaging with stakeholders) and, at the same time, grasping the opportunities offered by a governance model based on a broad vision of biobanks (i.e. a focus on society and the future of biomedicine and healthcare).

3.2. Clarification of the needs, goals and spaces of implementation for a good governance

The model of governance for biobanks in data-driven biomedical research that I propose is aimed to provide guidance for biobanks' stakeholders – defined as all those who have a role in regulating, designing, managing, using or participating in biobanks.[354] Such a model is aligned with the European framework of Responsible Research and Innovation that presents governance as a conceptual and practical structure that can foster research and innovation, taking into account ethics from the beginning to the end of the processes and whose direction is aligned with society's interests and expectations.

The process of conceptualising an appropriate model of governance for biobanks has required several progressive steps. First, as argued above, at a conceptual level, it is fundamental to adjust the focus of biobank governance and look at the question from the right perspective in order to gain a clear picture of what is at stake. For this reason, my proposal of a focus shift from a researcher-sample pair to a participant-data pair provides

[354] I have provided a complete list of biobanks' stakeholders in Chapter 1. They are participants, researchers, biobanks staff, patient organisations, disease-focused foundations, public institutions, private sectors and the general public.

the right theoretical framework on which to build the governance model and, at the same time, opens the door to progress in the form of adequate ethical guidance, because it allows us to examine the challenges of biobank governance in a data-driven research context.

Secondly, the next step is the assumption that an appropriate model of governance should reflect the actual needs of biobanks and should provide the conditions for their success. Therefore, on a more practical level, the process of conceptualisation moves from the following considerations: what is at stake for biobank governance in a data-driven biomedical context in terms of ethical, legal and societal challenges – in order to clarify actual needs, and the goals of biobank governance considering these challenges – that is, to clarify what is important for the success of a biobank.

Starting from the clarification of needs, from the analysis of the state of the art conducted in previous chapters, it can be maintained that the specific features of data-driven biomedical research that challenge biobanks and, thus, require specific action in terms of governance, are:

a) The trend towards the commodification of the human body and associated personal data that threatens the principle of non-commercialisation, the altruism associated with participation in biobanks and the focus on public good and shared benefit associated with research enterprise;[355]
b) The intensive digitisation of society and development of new technologies that could endanger the fundamental rights and freedoms of research participants and citizens; the potential misuse of personal data collected for research purposes that may result in covert discrimination and abuse of power against individuals and groups;[356]
c) The societal impact and loss of trust that may be generated by new risks associated with participation in biobanks created by digital society and fed by personal data; in particular, the possibility of linking different databases which may include personal

[355] N. Hoppe, K. Beier & C. Wiesemann, *Human tissue research: A European perspective on the ethical and legal challenges* (Oxford University Press 2011); I. de Lecuona Ramírez, 'La tendencia a la mercantilización de partes del cuerpo humano y de la intimidad en investigación con muestras biológicas y datos (pequeños y masivos)', Chapter 10 in M. Casado (ed.) *De la solidaridad al mercado: el cuerpo humano y el comercio biotecnológico* (Edicions de la Universitat de Barcelona 2017) 267–295. ISBN: 978-84-475-4193-5).
[356] I. De Lecuona, 'Pautas para evaluar proyectos de investigación e innovación en salud que utilicen tecnologías emergentes y datos personales' (2020) Informe del Observatorio de Bioética y Derecho, Barcelona.

data, including health and genetic data from biobanks, thus endangering participants' right to privacy.[357]

To these, we can add two more challenges that belong to a more conceptual level but have a concrete impact on practice:

d) A general lack of specific education, and informed debate and decision-making, regarding how data-driven biomedical research works and the requirements for research projects using personal data to be compliant with ethical standards.[358] This lack of knowledge may prevent the adequate protection of biobank participants' rights.[359]
e) The inadequacy of the research ethics framework to address the new challenges of biobank governance requires the ethical principles of the analogue society to be revisited in order that they fit the scope of digital society.[360]

Regarding the success of biobank governance, I argue that a contemporary model of biobank governance can be considered thriving if it can empower participants and society, ensuring adequate protection for participants and the implementation of ethical procedures while providing high-quality human biological samples and associated data to support biomedical research and innovation. This general statement can be broken down into specific goals for biobank governance:

a) Include mechanisms, practices and policies that ensure compliance with the principle of non-commercialisation of the human body and its parts – including associated data – promoted at the EU level. In particular, prevent biobank samples and data from

[357] K. Akyüz and others, 'Biobanking and risk assessment: a comprehensive typology of risks for an adaptive risk governance' (2021) Life Sciences, Society and Policy, *17*(1), 1–28; D. Rychnovská, 'Anticipatory Governance in Biobanking: Security and Risk Management in Digital Health' (2021) Science and Engineering Ethics, *27*(3), 1–18.
[358] I. de Lecuona 'Evaluación de los aspectos metodológicos, éticos, legales y sociales de proyectos de investigación en salud con datos masivos (big data)' (2019) Gaceta Sanitaria, *32*, 576–578; A. Ferretti and others, 'Ethics review of big data research: What should stay and what should be reformed?' (2021) BMC Medical Ethics, *22*(1), 1–13.
[359] C. Staunton and others, 'Appropriate safeguards and Article 89 of the GDPR: considerations for biobank, databank and genetic research' (2022) *Frontiers in Genetics*, *13;* D. Mascalzoni and others, 'Are requirements to deposit data in research repositories compatible with the European Union's general data protection regulation?' (2019) Annals of Internal Medicine, *170*(5), 332–334.
[360] C. Aicardi and others, 'Emerging ethical issues regarding digital health data. On the world medical association draft declaration on ethical considerations regarding health databases and biobanks' (2016) Croatian Medical Journal, *57*(2), 207.

being traded in exchange for money, with or by third parties, if collected only for research purposes.

b) Provide an adequate structure to mitigate the risks associated with biobank participants' loss of control over the use of their samples and data, due to the tendency of biobanks to collect prospectively, and new risks associated with the features of the digital paradigm. The goal is that participants feel protected and that their rights are respected, ensuring ethical governance of the entire life cycle of biological samples and associated personal data.

c) 'Demonstrate trustworthiness and accountability by orienting regulatory activities towards the ethically central interests at stake'.[361] Thus, according to the RRI's concept of public engagement, biobank governance must include mechanisms to foster alignment between how research is governed and stakeholders' values and interests in order to empower the latter through ethical procedures.

The final step in the conceptualisation of biobank governance is an acknowledgement of what is still missing in the process and where there is still space for further implementations, to ensure that the governance model is well-tailored.

The starting point for the process is that digital society has witnessed a paradigm shift in biomedical research that has brought transformative change in how biomedical research is conducted. This change is not yet adequately understood by society, ethicists and policy-makers and, thus, regulations and ethical guidance are inadequate.

To identify the changing requirements for biobank governance needed to push ethical and legal regulation forward, I turn to Aicardi and colleagues' analysis of shifts in the collection and use of health data and their implications for biomedical research.[362] At the same time, I maintain that an acknowledgement of the specific challenges brought by the digital paradigm to biobanks will lead us to see the protection of participants' privacy, informed consent and secondary uses as the most pressing ethical, legal and societal issues (ELSI) of biobanks in data-driven biomedical research.

[361] E. Vayena & A. Blasimme, 'Towards Adaptive Governance in Big Data Health Research' in *The Cambridge Handbook of Health Research Regulation* (2021) 257–265.
[362] Aicardi and others (n 49).

The first change to which biobank governance must adjust concerns the importance of understanding human biological samples as personal data. I have already argued for the need for a better understanding of the fact that, in the digital era, human biological samples are seen as a precious source of biological and genetic information. Two transformative features of the digital paradigm may have repercussions for the protection of biobank participants' data: first, the transferability of health data to other domains (and vice versa) in which 'virtually, any data set can be used to make health-relevant interferences pertaining to individuals (especially in the context of predictive analytics)' and 'the ownership of data and samples stored in a biobank can change and give rise to uses of data that were not intended by the biobank's initial mission';[363] secondly, the risks associated with predictive analytics in which 'it is very difficult, if not impossible, for individuals to know what data are used to make inferences and predictions about them. If data are used to harm them, or if inaccurate data are used, there are typically few options to rectify the harm/error or seek redress'.[364]

The second relevant change in data-driven biomedical research, one that profoundly affects biobank governance, is the limit to anonymisation. Indeed, as previously highlighted, the digital era has forced us to reconsider the notion that full anonymisation is a guarantee of the best protection and promotion of participants' interests and rights:

> Not only is the anonymity of data and material highly context-dependent, but data and material that are anonymized today may no longer be anonymous in the context of tomorrow's technologies and data resources. Whatever is contained in a health database, or a biobank may be anonymized and non-identifiable at the time it is set up, but this may not remain so over time, especially when data from the database or biobank are linked with other data sets.[365]

Thus, samples and data collected by biobanks are never fully anonymised and the re-identification of individuals is always possible.

The third change is the added pressure that certain features of data-driven biomedical research place on consent procedures. Indeed, 'when data are collected and stored for future uses, it is impossible to anticipate all future uses, and thus require fully informed and

[363] ibid. 208.
[364] ibid. 208
[365] ibid. 201.

specific consent'.[366] For this reason, in the context of biobanks, the classic model of specific consent – the consent to a specific study - must be replaced with a broader model of consent.[367] The main challenge for biobanks, in turn, in the context of data-centric research is to implement mechanisms of non-specific consent, but reliance on an opt-in model can be equally ethical.

Finally, another important reference in this attempt to understand the space for the implementation of biobank governance in data-driven biomedical research is the call made by Gille and colleagues analysing the conditions for 'future proofing' biobank governance. They have listed a set of conditions that biobanks should meet in terms of good governance to be prepared for their future in a context of data-intense research.

> We have shown that biobank governance relies on a variety of structures and mechanisms adopted across the board in a quite consistent way. We also stressed, however, that there is room for improving biobank governance especially in making accountability mechanisms more visible and adopting a systemic approach to oversight activities. Such adjustments are needed to future-proof biobank governance, to streamline the scientific exploitation of increasing amounts of data and biological resources, and to nurture public trust in science for the years to come.[368]

Finally, it goes without saying that the poor understanding of the methods, practices and risks that I have described above has brought with it an inadequate response in terms of ethical guidance. I aim to redress this in the next paragraph by proposing a set of principles

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[366] ibid. 208.

[367] The literature on the best type of informed consent in research biobank is extensive and the topic is the subject of ongoing debate. For an overview of the scope of the matter, see for reference:
T. Caulfield & J. Kaye, 'Broad consent in biobanking: reflections on seemingly insurmountable dilemmas' (2009) Medical Law International, *10*(2), 85–100; P. Granados Moreno & Y Joly, 'Informed consent in international normative texts and biobanking policies: Seeking the boundaries of broad consent' (2015) Medical Law International, *15*(4), 216–245; J. R. Karlsen, J. H. Solbakk & S. Holm, 'Ethical endgames: broad consent for narrow interests; open consent for closed minds' (2011) Cambridge Quarterly of Healthcare Ethics, *20*(4), 572–583; J. E. Lunshof and others, 'From genetic privacy to open consent' (2008) Nature Reviews Genetics, *9*(5), 406–411; J., Kaye and others, 'Consent for biobanking: the legal frameworks of countries in the BioSHaRE-EU project' (2016) Biopreservation and Biobanking, *14*(3), 195–200; K. S Steinsbekk, B. Kåre Myskja & B. Solberg, 'Broad consent versus dynamic consent in biobank research: is passive participation an ethical problem?' (2013) European Journal of Human Genetics, *21*(9), 897–902; J. Kaye and others, 'Dynamic consent: a patient interface for twenty-first century research networks' (2015) *European Journal of Human Genetics*, *23*(2), 141–146.
[368] Gille, Vayena & Blasimme (n 36).

that I believe are well-suited to tackling the challenges presented and fostering implementation.

4. The principles: transparency, data protection, participation

My goal is to design an ethical framework for biobank governance that ensures a balance between the beneficial applications of data-intensive biomedical research, understood as practices centred on the mass collection and processing of personal data, and adequate protection of biobank participants against the current risks and harms.

The proposed principles should not be considered as replacing rights to human integrity and dignity, privacy and confidentiality, the revocation of consent and not be discriminated against in health and genetic conditions, all of which underpin biomedical research ethics. However, I want to overcome the conceptual caution that usually accompanies the protection of research participants and, in recent decades, has led to an impasse in ethical guidance. In conceptualising an adequate ethical research framework for the digital era, we cannot risk overreacting in terms of ethical guidance and eventually re-establishing the primacy of the same principles that have proved to be inadequate in the face of new challenges.[369]

The principles that I propose are meant to support an appropriate model of biobank governance in the digital era are transparency, data protection and participation. They aim to meet the need for adequate ethical coverage in biobank governance in data-driven biomedical research and represent a move forward in the direction of bioethics for the digital age.

1) Transparency

The identification of transparency as a pivotal principle aligns with the current widespread acknowledgement that, in our digital society, transparently conveying relevant information about a given organisation is considered a basic principle of good governance in many sectors, biomedical research included.[370] A general and basic definition of transparency is

[369] B. D. Mittelstadt & L. Floridi (Eds.) *The ethics of biomedical big data* (Vol. 29) (Springer 2016).
[370] G.T. Laurie and others, 'Charting regulatory stewardship in health research: Making the invisible visible' (2018) Cambridge Q Health Ethics, 27:333–347.

the 'availability of information about an actor allowing other actors to monitor the working or performance of this actor'.[371]

To comply with this principle, biobanks must make the entire process of biobanking transparent – from the collection of samples and data to the moment when external researchers deliver their discoveries to the scientific community based on biobanks' resources.

To date, there are few studies related to the conceptualisation and implementation of transparency in biobank governance and, as in the case of the Taipei Declaration, the descriptions of the goals that the application of the principle should achieve are poor.[372] The aforementioned work of Gille and colleagues represents a valuable exception that provides an important insight into the scope of the principle of transparency for biobank governance:

> Transparency enables donors to better understand how a biobank is governed and therefore to make better, more informed decisions about donation and research participation. More specifically, transparency about governance mechanisms is critical for biobanks to be perceived as responsible and trustworthy actors, especially when those biobanks are supported through public funds and aim to uphold privacy and ethical standards for the retention and use of public and patient tissue samples.

For biobanks, being transparent about governance also facilitates accountability, the combination of actions through which an organisation makes itself answerable for its operations, that is, capable of accounting to its stakeholders for the actions it has undertaken.[373] According to Gille and colleagues, for a biobank, 'being accountable implies providing information providing relevant information about how samples and data are stored, used and shared; answering stakeholders when they ask for explanations about its conduct; and be under the condition of being affected by stakeholders' judgment of its operations'.[374]

In accordance with the broad vision of the biobank and the focus on participants and data embraced by my model of governance, I argue for a minimum level of transparency to be

[371] A. Meijer, 'Transparency' in M. Bovens, R. E. Goodin & T. Schillemans, (eds.) *The Oxford handbook of public accountability* (Oxford University Press 2014).
[372] Gille, Vayena & Blasimme (n 36).
[373] M. Bovens, 'Two concepts of accountability: accountability as a virtue and as a mechanism' in D. Curtin, P. Mair, Y. Papadopoulos (eds) *Accountability and European governance* (Routledge 2014).
[374] Gille, Vayena & Blasimme (n 36).

respected. Specifically, governance mechanisms should be implemented in all stages of biobanking to ensure transparency in i) how collected samples and data are collected, stored and shared; ii) how participants' personal data are treated; iii) who is given access to biobank data and samples; iv) the criteria that inform Access/Ethics committees; v) what kind of research this access supports; vi) whether private and for-profit companies are given access to samples and data, and under what conditions; and vii) the obligations of researchers after receiving the biobank resources.

In this respect, the study conducted by Gille and colleagues provides important insights into the gaps in the implementation of standards of transparency in biobank governance and accountability mechanisms. They propose specific actions to address this:

> Address stakeholders (such as sample and data donors, biobank users, members of the biobanking community, public and private sector scientists and institutions, and the lay public) at an appropriate language level and format and keep this information up to date; Collect public feedback about existing governance activities, including transparency strategies; Help nonexperts to understand the information you provide; Implement transparency strategies with a clear purpose; Stimulate public awareness about biobanking through dedicated campaigns and outreach activities; Target lay community with transparency strategies to increase trustworthiness.[375]

Beyond its practical implementation, it is worth considering at this point how well-suited the principle of transparency is to tackle the challenges of biobank governance identified above. Firstly, the principle of transparency is intended to make biobanks accountable for each operation, decision and behaviour concerning stakeholders; in turn, this ensures participant and public trust in the biobank. I argue that if the principle of transparency is paramount in informing the model of biobank governance, and all the processes for collection, storage, sharing, access criteria, Committees' assessment, return of results and relationships with the private sectors are genuinely transparent, then participant protection and empowerment are ensured. This is a key goal of biobank governance, as listed above. Once the implementation of transparent mechanisms is achieved at all levels of biobank governance, the most difficult knot in the biobank's ELSI can be untangled. The principle of transparency

[375] F. Gille, R. Axle & A. Blasimme, 'Transparency about governance contributes to biobanks' Trustworthiness: call for action' (2021) Biopreservation and Biobanking, *19*(1), 83–85.

is well-suited to tackle the challenges for biobanks raised by the digital paradigm, namely the risks from re-identification, transferability to third parties, linking of datasets and limits of consent procedures due to the re-use and re-purposing of data. Therefore, transparency, on the one hand, meets the needs of participants and the public 'for a better understanding of how data are governed and protected against intentional and unintentional privacy breaches, or how data are shared with third parties and linked with other data sets'.[376] On the other hand, a clear and manifested commitment of biobank governance towards transparency can be acquired as a valid complement to informed-consent practices (open, broad, blanket). This can also be achieved by requiring researchers to return results to the biobank and acknowledge the biobank from which the samples and data originated in scientific publications.

Secondly, transparency, and in turn accountability, about the biobank's access policy and the decision-making processes of ethics/access committees (those committees that usually assess requests to use biobank resources for research projects) is a strong instrument to prevent biobank samples and data being traded in exchange for money by third parties without the knowledge of participants or the general public. Indeed, since we can expect that participants and the public are averse to the commodification of biobank resources, and that such use may deter them from future participation, biobanks must disclose who has been given access to specimens and also how requests for access are handled when financial interests are detected. As argued by Spector-Bagdady and colleagues, such disclosure will enable participant autonomy via increased transparency, allowing prospective contributors to make the most informed decision for themselves.[377] In this way, informed by the principle of transparency, biobank governance can respect the altruistic motivation of present and potential participants and the research-oriented framework in which samples and data are initially collected – which is another goal of biobank governance identified above.

2) Data protection

The principle of protection needs to be understood as a manifestation of the commitment of biobank governance towards the implementation of and respect for adequate safeguards

[376] ibid, 2.
[377] K. Spector-Bagdady and others, 'Encouraging participation and transparency in biobank research' (2018) Health Affairs, *37*(8), 1313–1320, p. 1319.

when managing biobank participants' personal data.[378] For this reason, this principle is closely related to how biobank governance builds oversight mechanisms and samples and data access policy. It is also a response to the current fragmented regulatory situation regarding biobanks across Europe. This situation presents the right conditions to demonstrate how biobank governance involving a complex and decentralised system of actors and mechanisms is an adequate example of post-regulatory governance that can fill the gap left by an inadequate response by the law.[379]

The inclusion of the principle of data protection in my model of governance responds also to the need to fill a lack of understanding of the digital paradigm at different levels (i.e. among researchers, participants, private partners, public institutions and the general public) and raise awareness of the fact that biobank resources need to be protected as personal data in legal and ethical policies and guidelines. I argue that the next step in providing adequate protection to biobank participants in the digital paradigm is – at the level of the infrastructure (top-down) – to ensure that all actors are able to identify the ethical issues in everyday practice beyond mere legal compliance. Conversely, at the level of the participant (bottom-up), donors, participants, citizens, the public and society, in general, need to be clear on the ethical, practical and legal implications of signing informed consent. For example, if I sign an open informed consent, I need to understand clearly that my samples and data may be used for unforeseen research.

In Chapter 1, I conducted an analysis of biobank regulation and concluded that there is insufficient clarity on what constitutes an adequate safeguard when processing personal data under the exemptions to GDPR provisions for research:

> Article 89(1) of the GDPR states that safeguards 'shall ensure that technical and organisational measures are in place in particular in order to ensure respect for the principle of data minimisation'. These measures 'may include pseudonymisation, but offer no further insight into what they may also be'.[380]

[378] Staunton and others (n 48).

[379] Gille, Vayena & Blasimme (n 36).

[380] C. Staunton, S. Slokenberga & D. Mascalzoni, 'The GDPR and the research exemption: considerations on the necessary safeguards for research biobanks' (2019) European Journal of Human Genetics, *27*(8), 1159–1167. p. 1163.

Staunton and colleagues have argued 'that a full implementation of the derogations as provided for under the GDPR may render the research unethical and not in line with individuals' interests'.[381] In the specific case of biobanks, indeed, data subjects – being stripped of a number of rights – are aware of the processing of their data for biobank research (after having signed an informed consent form), but may have no right to access information on this research, or to object to the research, or to restrict the use of their data for secondary uses, hence the importance of implementing appropriate governance mechanisms for participant protection in biobanks. I refer here to adequate oversight procedures and mechanisms that a biobank needs to put in place to monitor its own operations in the interests of affected parties.[382] In particular, this concerns the definition of the criteria informing the decision-making of the committees[383] appointed to assess access requests for biobank resources.

I argue, in accordance with the literature on the ethical acceptability of specific data access requests in the field of biomedical research[384] that, as a minimum, adequate protection for biobank participants' samples and data is reached through:

i) adequate criteria for the project's assessment:[385] the scientific validity, quality and potential of the proposed research project; the CV and bona fides of the researchers requesting the resources; a clear explanation of how projects will comply with the principles of data minimisation, how data will be used and where will it be stored and for how long, who is responsible for coordinating the data processing; monitoring measures implemented by the final recipient for the use of personal data in the hands of researchers, promoters and other parties with access to the biobank's datasets;[386]

ii) clear restrictions about re-use and re-purposing of data with respect to informed consent, and specific policies against commercial uses;

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[381] ibid. 1166.

[382] E. Vayena & A. Blasimme, 'Health research with big data: time for systemic oversight' (2018) Journal of Law, Medicine & Ethics, *46*(1), 119–129.

[383] Depending on the governance structure of each biobank, this appointed committee may be a Research Ethics Committee of the research institution hosting the biobank, a Data Access Committee in the context of genetic and genomic data sharing or an external ethics committee.

[384] M. Shabani and others, 'Oversight of genomic data sharing: what roles for ethics and data access committees?' (2017) Biopreservation and Biobanking, *15*(5), 469–474; K. C. O'Doherty and others, 'Toward better governance of human genomic data' (2021) Nature Genetics, *53*(1), 2–8.

[385] D. Mascalzoni and others, 'International Charter of principles for sharing bio-specimens and data' (2015) European Journal of Human Genetics, *23*(6), 721–728.

[386] de Lecuona (47)

iii) a clear position on the return of results and incidental findings to participants.

In the absence of regulatory consistency around international data sharing in biobanking, and faced with a lack of harmonisation about what constitutes ethical safeguards, I believe that including data protection among the principles that inform biobank governance is the best way to tackle the principal challenges facing biobanks in data-driven biomedical research. In particular, establishing and transparently communicating biobank policies about commercial use addresses the tendency towards the commodification of biobank samples and datasets. Furthermore, the implementation of well-tailored oversight mechanisms is a way to mitigate the risks associated with the re-use and re-purposing of participant data, especially when the data subject has not provided specific consent to such use of the data.

As regards the goals of biobank governance, I maintain that the principle of data protection reflects the goal of preventing biobank resources to be traded in exchange for money by third parties and mitigates the risks associated with biobank participation.

3) Participation

By participation, I mean the involvement and engagement[387] of the greatest possible number of biobank stakeholders in biobank governance. In particular, I refer to the inclusion of participants, patient advocates and lay members as representatives of the general public to attain the alignment between research governance and societal interests that I have identified as one of the goals of biobank governance and that is promoted by the concept of public engagement in an RRI framework.

I believe that the current problem with participation in biobanks is that the scope is not well defined; no guiding ethical principles have been developed, just a set of strategies to encourage citizens to participate in biobanks with samples and data and to support the biobank mission. Thus, in order to understand the conditions for implementing the principle of societal participation in biobank governance, it is a priority to define the scope of participation in biobanks themselves.

I will first provide some background on biobanks and participation. The literature on the topic shows that – despite many references to public engagement and participants' inclusion in the domains of biomedical research, clinical trials and genetics research – significant

[387] In what follows, the terms 'participation', 'engagement' and 'involvement' will be used interchangeably.

confusion remains around the kind of practices that can be considered 'participatory' in biobanks[388]. Nevertheless, since these participatory claims imply promises of a new role and commitment for participants, clarifying the significance of participation in biobanks is necessary and urgent to avoid two likely negative consequences:

a) A merely *pro forma* involvement, where the role played by participants is exclusively instrumental for the sake of biobanks' public legitimation or a way to exploit participants' goodwill and engagement to obtain additional resources and enhance reputation;

b) Poor management of their interests and roles, possibly discouraging future involvement and creating a general mistrust of the work of biobanks.[389]

The appeal to participatory forms of biobanks governance reflects the general shift toward a patient-centred approach in biomedical and genetics research.[390] This has reached the biobanking field due to the increasing demand for biobank resources to foster data-driven biomedical research that, in turn, has brought a recognition of biobanks as a research asset, whose participants represent precious repositories of biospecimens and data, and which deserve to be approached as research partners.[391]

For the purposes of this proposal, I argue that including the principle of participation in the ethical framework brings two important benefits to biobank governance, aligned with the goals identified above. The first benefit is the recognition of the value that participants, patient advocates, disease-oriented foundations, civic associations and the general public can bring as stakeholders in governing a biobank;[392] the second is a particular effort to listen to the participant's voice and enhance the interests of participants and the rest of society by involving them in the decision-making processes concerning the collection, analysis and circulation of their samples and data.[393]

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[388] de Lecuona (n 47).
[389] K. Beier, M. Schweda & S. Schicktanz, 'Taking patient involvement seriously: a critical ethical analysis of participatory approaches in data-intensive medical research' (2019) BMC Medical Informatics and Decision Making, *19*(1), 1–10.
[390] J. Kaye and others, 'From patients to partners: participant-centric initiatives in biomedical research' (2012) Nature Reviews Genetics, *13*(5), 371–376.
[391] E. Elenko, L. Underwood & D. Zohar, 'Defining digital medicine' (2015) Nature Biotechnology, *33*(5), 456–461.
[392] D. Mitchell and others, 'Biobanking from the patient perspective' (2015) Research Involvement and Engagement, *1*(1), 1–17.
[393] A. Blasimme & E. Vayena, 'Becoming partners, retaining autonomy: ethical considerations on the development of precision medicine' (2016). BMC Medical Ethics, *17*(1), 1–8.

In other words, I believe that the principle of participation reflects the goal of biobank governance to implement strategies better aligned to the needs of biomedical research (concerning biobank samples and data) and the interests of society. Furthermore, biobanks' commitment to societal participation in their governance – in particular regarding the lay public and participants – demonstrates a willingness to take into account ethically central concerns in terms of societal interests.

To achieve this goal and find the best way to implement the principle of participation in biobank practice, it is important to clarify the roles, played by various individuals, which are called into question when dealing with participatory forms.

Of course, this clarification is strictly dependent on the type of biobank in question. For instance, when dealing with disease-oriented biobanks, samples and data are usually provided by patients who become involved with biobank activities to discover the cause of their disease and improve their health. In this context, patients are usually represented by patient organisations composed of patients, relatives or patient advocates. In contrast, in the case of population-based biobanks – which collect and organise samples and data from healthy donors – participants are recruited from the general public who contribute to the research for various reasons, ranging from solidarity to trust in the scientific process.

According to the principle of transparency, each biobank should make clearly available information on how they intend to involve participants in their governance. To date, the activities where participants and the general public can be involved in biobanking range from protocol design, criteria for recruitment, feedback on research findings, direct access to data and assessment of results. However, the degree of involvement and the range of practices rarely reach the threshold of a basic level of participation that is limited to the phase of recruitment, the collection of samples and data, and informed consent procedures.

I suggest that two further levels of participation be considered. The first is interactive engagement through dynamic consent, which is designed to enable biobank participants to revisit their consent choices and have an updated overview of the biobank's activities and the research for which their samples and data are being used.[394] This type of participation

[394] M. Prictor, H. J. Teare & J. Kaye, 'Equitable participation in biobanks: the risks and benefits of a 'dynamic consent' approach' (2018) Frontiers in Public Health, 253; J. E. Pacyna and others, 'Assessing the stability of biobank donor preferences regarding sample use: evidence supporting the value of dynamic consent' (2020) European Journal of Human Genetics, *28*(9), 1168–1177.

would address concerns about open consent and secondary uses of samples and data. In turn, the resulting value is improved trust on the part of participants (they have greater trust if there is ongoing engagement) and an increased degree of transparency and accountability for the biobank.[395]

Another potential level is the involvement of participants and the general public in governance structures. This level of participation reflects the need to value the voices and interests of participants and society and to allow them to contribute to decision-making processes. In particular, by sitting on a biobank's Access or Ethics Committee, participants and other representatives of society can contribute to the assessment of requests. In particular, their voices are valuable concerning local research priorities, the ethical sustainability of the proposed research and the likely benefits of the research to patients and public.[396]

To conclude, I maintain that the principle of participation is well-suited to tackle the challenges of biobank governance in the digital society because it responds to the opportunity offered by the digital age and the datafication of our health to become 'active partners' as regards personal health data; in a world where it is common for citizens to share their genetic and health-related personal data through mobile devices and apps, allowing them to be more involved in biobank projects is easily achieved.

At the same time, in the specific context of biobanks, the principle of participation is intended to mitigate the loss of control over biobank samples and data that participants may experience as a result of open informed consent, secondary uses and the risks associated with privacy due to the transferability and linking of data sets and predictive analytics.

In terms of the goals of biobank governance, the principle of participation reflects the need to orient biobank activities towards the ethically central interests of society and, in turn, find

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[395] R. Biasiotto, P. P. Pramstaller & D. Mascalzoni, 'The dynamic consent of the Cooperative Health Research in South Tyrol (CHRIS) study: broad aim within specific oversight and communication' (2021) BioLaw Journal-Rivista di BioDiritto, (1S), 277–287; S. E. Wallace & J. Miola, 'Adding dynamic consent to a longitudinal cohort study: A qualitative study of EXCEED participant perspectives' (2021). BMC Medical Ethics, *22*(1), 1–10.

[396] B. K. Myskja, 'Lay expertise: why involve the public in biobank governance?' (2007) Genomics, Society and Policy, *3*(1), 1–16; A. K. Hawkins & K. O'Doherty, 'Biobank governance: a lesson in trust' (2010) New Genetics and Society, *29*(3), 311–327; L. Luna Puerta and others, 'The reported impact of public involvement in biobanks: a scoping review' (2020) Health Expectations, *23*(4), 759–788; S. Erikainen and others, 'Public involvement in the governance of population-level biomedical research: unresolved questions and future directions' (2021) Journal of Medical Ethics, *47*(7), 522–525.

the right alignment between how biobanks are governed and society's values and expectations.

To conclude this presentation of the ethical framework that I propose in order to guide biobank governance in data-driven biomedical research, I argue that the ultimate goal in the application of the proposed principles is to increase society's trust in biobanking endeavours. Just as respect for the rights of human integrity, privacy, confidentiality and non-discrimination is necessary to build trust and develop valuable relationships between research participants and the research system, a greater degree of transparency – as well as a guarantee of data protection through adequate oversight mechanisms and a proper participation framework – is necessary to build participant and public trust in biobanks' activities, even in the face of the greatest challenges brought by the digital paradigm.

Furthermore, I want to mention the importance of the relationship between these proposed principles. They must be considered as a united framework, but the order in which I have proposed them is important – it is no coincidence that transparency occupies the first place. I argue that from the point of view of the public and prospective participants, the decision to participate by allowing their samples and data to become part of a biobank is subject to a belief that their rights are protected. However, this feeling of protection comes from a previous acknowledgement of the transparency of the processes involved and depends on these being adequately communicated and explained. This is of particular importance in the face of new conditions of informed consent due to the changing requirements brought by the digital paradigm.

Having proposed a model of biobank governance that embraces a vision of the biobank as society-oriented and as a testing ground to rethink research ethics, the proposal to prioritise transparency, participation and protection is, I believe, a way to respond to and fight the detrimental tendencies of current scientific assets. The current approach to the governance of biomedical research does not yet have an adequate level of social engagement or sufficiently transparent mechanisms to avoid misconceptions among the general public about how research is conducted and governed. If we continue along this path, we run the risk that the participatory space opened by the digital society becomes an arena where

everyone can speak without a thorough understanding of the practices or what is at stake in terms of ethical, legal and social issues.[397]

In contrast, I argue that if transparency, protection, participation and the resulting general trust in biobanking activity are not prioritised as principles for biobanks' 'good governance' and biomedical research governance, we run the risk that the wrong priorities and values will guide how biomedical research is conducted (e.g. market priorities and technological solutionism) and how it is perceived by society, and we will lose the opportunity to orient biomedical research towards what is ethical central for society.

[397] For a critical analysis of the management of the emergence of COVID-19 in Italy, see S. Camporesi, F. Angeli & G. D. Fabbro, 'Mobilization of expert knowledge and advice for the management of the Covid-19 emergency in Italy in 2020' (2022) Humanities and Social Sciences Communications, *9*(1), 1–14.

5. Conclusions

In this chapter, I was finally able to address the main research question of my dissertation, namely what the most suitable governance model for biobanks is, to foster research and innovation in the growing field of data-driven biomedical research in such a way that this governance is centred on the ethically central issues and aligned with the needs of research participants and wider society. To answer this question, I have structured this chapter in two parts, corresponding to deconstruction and construction.

In the first part of this chapter, I laid the ground for the proposal of a model of governance based on principles of transparency, data protection and societal participation by providing a conceptual structure following a line of reasoning based on two main arguments. First, the analysis that I have conducted on the phenomenon of the biobank on four levels[398] has proven that the more we enlarge its focus from a basic understanding of the biobank as a repository of biospecimens and associated data, the richer and the deeper becomes the space for reflection on the significance and importance of conceptualising an appropriate governance model for biobanks. This is because reflection on biobank governance today touches on some of the most crucial questions in the areas of ethics and the regulation of data-driven biomedical research.

Secondly, I have claimed that the best model of biobank governance in the digital society is one that conveys a broad vision of the biobank, socially and participant-oriented and allowing all the ELSI related to biobank activities in the digital society the attention they need. I have come to this conclusion by juxtaposing this vision of biobank with another that is more medical-oriented, based on an understanding of biobanks merely as biomedical repositories and research infrastructures, and strongly anchored to conventional biomedical research ethics and one that in my opinion must be dismissed.

In the second part of the chapter, I have first maintained that the best approach to biobank governance in the digital society is based on a focus shift from a researcher-sample model to a participant-data model. Only by acknowledging this shift will we have the opportunity to include in the discussion specific features and challenges brought by the digital society to biobanks, including in the discussion a larger number of stakeholders along with their

[398] First level: the biobank as a repository of human biological samples and associated data; Second level: the biobank as a research infrastructure; Third level: the biobank as a vantage point for the governance of data-driven biomedical research; Fourth level: the biobank as a testing ground for revisiting research ethics.

expectations and priorities for biomedical research governance. In particular, this focus shift allows the inclusion also of patients and participants as biobank users, recognising the centrality of data in biobanks and extending the beneficiaries of the research derived from biobanks to encompass society as a whole.

Then, I presented in detail the process that I have undertaken to conceptualise an adequate model of governance for biobanks. This process comprises two parts. First, I have clarified the key challenges in governance in the digital society, its goals and spaces of implementation. Accordingly, I have maintained that, in order to be successful, biobank governance must aim to prevent biobank samples and data collected for research purposes from being traded in exchange for money with third parties without the participants' knowledge, to mitigate the social impact of digital and technological advances on participants' rights and freedoms and to demonstrate trustworthiness towards society by orienting its practices, procedures and policies towards what is considered ethically central for both society and participants.

Secondly, having identified the challenges and goals for biobank governance, I have argued that three principles should inform the model of governance to provide adequate ethical protection for biobank participants and for biobank practices to be considered ethical: transparency, data protection and participation. I have maintained that each of these principles is well suited to tackle the challenges and to enable biobank governance to reach its goals. In particular, I believe that they can make a difference in addressing what I have identified as the most pressing biobank ELSI in the digital age: privacy, informed consent and secondary use.

Thus, the principle of transparency is intended to hold biobanks accountable for each operation, decision and action implied in the processes of collection, use and sharing of participants' biological samples and personal data. I have argued that if the governance of the entire cycle of samples and data – from the needle to the freezer, from the freezer to the lab and from the lab to society – is completely transparent, then the ELSI raised by the lack of specific consent and unwanted secondary uses are mitigated.

The principle of data protection reflects the biobank governance goal to mitigate the risks brought by the digital paradigm to participants' rights and freedoms, such as covert discrimination and the abuse of power when dealing with personal data. In turn, I have

argued that this principle accommodates the cluster of ELSI that arise around privacy associated with biobank participation.

Finally, the principle of participation is well-suited to support biobank governance in complying to orient biobank activities towards the ethically central interests of society and, in turn, finding the right alignment between how biobanks are governed and society's values and expectations. It responds also to the need to accommodate biobanks' ELSI by putting forward conditions – in terms of a governance structure – for social scrutiny and monitoring, by creating the right space for public engagement and the direct involvement of participants.

In conclusion, I believe that in the face of an extremely fragmented regulatory situation for biobanks across Europe and of the inadequacy of a research ethics framework that needs to be rethought to tackle the challenges of the digital paradigm, the model of biobank governance that I have presented in this chapter should be considered a conceptual basis for the implementation of a national and international normative framework of biobanks. From an ethical perspective, I have demonstrated that the current ethical and legal framework that informs biobank governance has not kept pace with the transformative developments of the digital era and, for this reason, my proposal should be read as an attempt to lay the foundation for an urgent adjustment of the legal and ethical normative framework that governs biobanks.

Conclusion

The greatest challenge for biobanks in the digital age is to keep pace with the promising narrative surrounding their key role in fostering the goals of data-driven biomedical research. In this dissertation, I have attempted to adjust this narrative by demonstrating that real success for biobanks in the digital era is to be found in promoting an ethically and socially desirable direction for biomedical research and innovation while supporting the need of the scientific community for human biological samples and associated personal data. Accordingly, I can now make some final considerations about the concrete contribution of the present work to the conceptualisation of a proper model for biobank governance in the digital society.

1. **The way in which biobanks are regulated by the ethical and legal framework in Europe is not sufficient to support the expectations and the challenges attached to biobanks in data-driven research. For this reason, I propose to focus on the governance of biobanks as a way to promote ethical practices associated with the collection, use and sharing of human biological samples and associated personal data**.

This dissertation faces the difficulty of reaching a common understanding of what constitutes governance, given that its definition can vary depending upon the field discussed. My analysis aimed to demonstrate that the governance of biobanks in the digital society – to be truly ethical and aligned with societal interests – needs to be understood as broader than simply a system of ethical oversight and the accountable distribution of roles and responsibilities. In line with the European framework of Responsible Research and Innovation, I proposed a concept of governance as a structure in which ethics and public engagement pursue the same aims of promoting ethical practices in the collection, use and sharing of human biological samples and personal data for patient, participant and societal interests. Moreover, to research this goal I propose elevating the concept of governance beyond legal compliance with regulations to engage with a continuous moral evaluation of practices over and above the application of the formal rules that often are inadequate to guarantee appropriate ethical safeguards for biobank participants.

2. **The ethical principles informing biobank governance need to be adapted to compensate for the need for specific consent as a guarantee of individual autonomy and the risks to participants' rights and freedoms in the face of the fact that the traditional research ethics framework was conceived to support biomedical research and protect participants within an analogue society. This is, in turn, inadequate for the current situation**.

My contribution must be read as aiming to add a specific value to the ethics of biobanking but in line with this understanding of secular bioethics anchored to human rights, and respect for participants' rights and freedoms. For this reason, my proposal to conceptualise a new ethical framework for biobanks – that, in my vision, is also a testing ground for bioethics for the digital society – based on the principles of transparency, data protection and participation, must be read in line with the inalienable human rights and freedoms promoted by the international framework provided by the UNESCO Declaration on Bioethics and Human Rights, the Council of Europe Convention on Human Rights and Biomedicine, and the WMA Helsinki and Taipei Declarations, which provide certain and common reference points on how biomedical research must be conducted to reach the threshold of ethical standards.

3. **A focus shift from the researcher- samples model to a participant - data model is proposed to move away from an understanding of biobank as being just medically-oriented so as to reach an understanding of governance that is societally and participatory oriented is needed.**

My proposal is to overcome a narrow and purely medically oriented vision of the biobank as at the service of biomedical research, and to shift the focus from researchers to participants, and from the sample to the associated information that goes far beyond the sample itself. Only with this change in perspective, does it become possible for biobank governance to consider what is important in terms of societal interests in biobanking and biomedical research in the face of the specific features of data-driven biomedical research and society. That is, by participating in a biobank, the crucial ethical issue for society and, specifically, participants, is the protection of genetic and health-related data from the risks related to secondary use, commercial use and covert discrimination. Such risks are associated with technological advances characteristic of the digital paradigm, such as the possibility of the

re-identification of encrypted data and the consequent risk to privacy, and the risks associated with the personal data marketplace, that is, the possibility that health-related data collected for research purposes may be sold to third parties without participants' knowledge. Moreover, what I believe is central for biobank governance to remain aligned with societal interests and implement an ethical way to collect, use and share personal data attached to samples, thereby respecting the values associated with research participation and goals – benefit-sharing, the common good, solidarity and respect for the 'given word'; that is, if samples and data are collected for a specific purpose, even a very broad one, biobanks and researchers should not break the trust placed in them by society. Accordingly, understood in this way, biobank governance becomes a concrete instrument to fight the tendency towards the commodification of samples and data which harms the research system and contributes to the loss of trust in the research by the society.

4. **The main outcome of my proposal is a framework of three principles that can provide an adequate ethical coverage for biobank participants based on the proposed vision of biobank broader than just a medical repository and open towards the society**.

The principles of transparency, data protection and participation are intended to mitigate the most pressing biobank ELSI identified in the digital society – privacy, informed consent and secondary uses.
The principle of transparency is intended to make biobanks accountable for each operation, decision and behaviour implied in the processes of collection, use and sharing of participants' biological samples and personal data. If the entire governance of the cycle of samples and data – from collection to the disclosure of results – is completely transparent, then the ELSI arising from lack of specific consent and potential misuse are mitigated. The principle of data protection reflects the focus on participants and data embraced by my model and it is intended to mitigate the risks to participants' rights and freedoms brought by the digital paradigm, such as covert discrimination and abuse of power when dealing with personal data. Finally, the principle of participation responds also to the need to accommodate biobanks' ELSI in proposing conditions for social scrutiny and monitoring by creating an appropriate space for public engagement and participants' direct involvement. My proposal must be understood as an integral part of an interdisciplinary approach to which my contribution provides the conceptual analysis that has integrated an analytic approach derived from philosophy with inputs from other disciplines such as law, medicine and

computer science to redefine the problem and look at the issues from a most helpful perspective.

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